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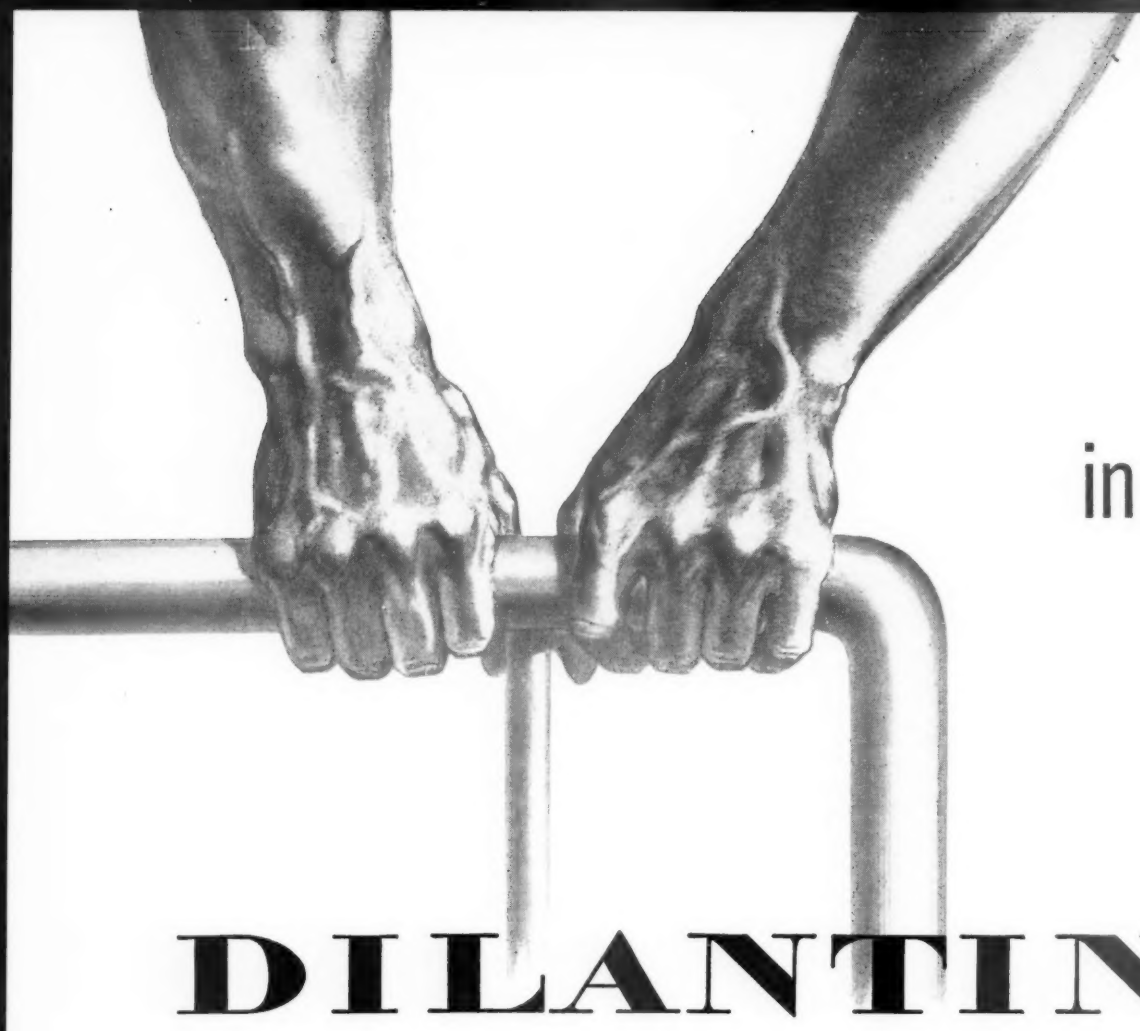

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GUEST EDITORIAL

Factors Concerned with Prognosis of Acute Myocardial Infarction

IT HAS been thirty-nine years since Herrick's classical description of coronary artery occlusion was published. All clinicians have become familiar with the high mortality incidence and the great frequency of thrombo-embolism seen in this syndrome.

When the fundamental architecture of the coronary circulation is borne in mind it is easy to understand why there must be much uncertainty in the prognosis. In a physiological sense the coronary arteries are end-arteries, even though there are inter-communications between the three main coronary branches. Therefore, the occlusion of a major artery is followed by death of the muscle which it supplies. Furthermore, there is marked variability in the coronary outflow from patient to patient. This varies between thirty and ninety per cent of the inflow in a normal individual. The drainage into the right heart occurs via the coronary sinus, the accessory coronary veins and by way of the numerous thebesian vessels. These thebesian channels are very scant in the left ventricle which accounts for the fact that ninety-eight per cent of all infarctions occur on the left side of the heart. These rare right infarctions may occur when mural thrombi obstruct the thebesian drainage into the right ventricle. With this fundamental cardiac anatomy in mind, it is not safe to predict the outcome in any single individual following an attack of acute coronary occlusion.

In a recent review of four hundred consecutive patients, two hundred and ninety-two of whom were treated with anticoagulants, it has been possible to draw some conclusions as to the immediate prognosis. The elevation of the total white blood count and the degree of elevation of the rectal temperature perhaps reflect the extent of necrosis following the occlusion of a vessel. When the rectal temperature persisted above one hundred and two degrees in this group of patients the mortality incidence was sixty per cent. In those patients with a white blood count exceeding fifteen thousand, the death rate was double the normal mortality incidence.

The age of the patient bore a direct relation to the prognosis. Eighty-five per cent of the deaths in these patients occurred between the ages of fifty and sixty-five. No deaths occurred under the age of thirty and two deaths occurred under the age of forty.

In those patients who were hospitalized for their first attack, the mortality rate was fourteen per cent as compared with an incidence of thirty-one per cent who had two myocardial infarctions. The death rate in those patients who had three or more clinical occlusions was fifty per cent. In other words, the greater the extent of myocardial damage for any given patient the higher we must expect the mortality rate to be.

Peripheral thrombo-emboli occurred in fifteen per cent, and of this special group, one-half died. In the group who had anticoagulants, embolism occurred in six per

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cent. On the basis of these data, thrombo-emboli occurring subsequent to a coronary occlusion presented a serious hazard to the patient. These emboli occurred in the cerebral arteries, mesenteric vessels and the pulmonary system—one-half occurring in the latter circuit.

One-fourth of the deaths occurred during the first twenty-four hours due to shock and arrhythmia. Rupture of the heart occurred in two patients. The appearance of arrhythmia of the heart, not including extra systoles, was a frequent complication. When ventricular rhythm occurred the prognosis was exceedingly grave. This complication was recorded electro-cardiographically in two per cent and death occurred in all, with two exceptions. The mortality incidence was slightly higher in the females and in those with a history of hypertension.

With anticoagulants the mortality incidence was seventeen per cent, which is not as favorable as the incidence reported by Wright. It is hopeful that this rate may be reduced by improvement in future therapy, with particular reference to the use of more dependable anticoagulants. The judicious use of oxygen, morphine with atropine and papaverine were important aids in the saving of lives.

MARSH MCCALL, M.D.

Dr. McCall is a graduate of the Medical College of Virginia, Class 1930, and is now Chief of the Medical Service at the Beekman-Downtown Hospital, New York City.

Bibliotheca Obstetrica

[HILL (SIR JOHN) 1716-75.]

LUCINA SINE CONCUBITU. A Letter Humbly address'd to the Royal Society; in which is proved by most Incontestible Evidence, drawn from Reason and Practice, that a woman may conceive and be brought to bed without any Commerce with Man. First Edition, *London, M. Cooper,* 1750.

The extremely scarce first edition of Hill's famous skit, directed against the Royal Society when they refused him a nomination for fellowship. Osler had only the first edition in French, and notes that the earliest English edition he can trace in the British Museum, Surgeon General's Catalogue and other libraries is the second. The tract was signed: "Abraham Johnson".

Osler has the following to say about the author: "Beginning as an apothecary, Hill became a playwright and actor, a journalist, and a translator. He obtained a medical diploma from St. Andrews and his knighthood from Sweden. He was a versatile, unscrupulous man, with considerable abilities, great perseverance, and unlimited influence. Most of his books (84 are listed in the D.N.B.) are trashy compilations, but some of his botanical works did good service, and the first Linnean flora of Britain was due to him." Garrick wrote on Hill the well known epigram:

"For physic and farces his equal there scarce is;
His farces are physic, his physic a farces is."

CHRONIC LUNG FAILURE*

John L. Guerrant, M.D.,†
Charlottesville, Virginia.

Lung failure is a common condition but the term is not often used and its presence is often overlooked. It is frequently confused with either heart failure or asthma. The confusion with heart failure is due to the fact that the major symptom of lung failure, exertional dyspnea, makes doctors as well as patients think of heart disease. It is confused with asthma because so many patients with lung failure wheeze. Every physician should be able to differentiate chronic lung failure from heart disease, from asthma, and from other causes of chronic dyspnea. The purpose of this report is to define and discuss lung failure, to state the criteria by which it may be differentiated from other causes of chronic dyspnea, and to describe some useful methods of treatment.

A single normal respiration consists of a complicated chain of events initiated by an impulse arising in the respiratory center and ending when blood saturated with oxygen leaves the alveolar capillary[1]. Table I shows the links in this chain. Respiratory failure is likely to accur if the chain is weakened or broken at any point. The break may be due to various diseases. Common examples are a hemorrhage into the respiratory center or a perforating wound into the pleural space. If the disease is a chronic one that involves the lung itself or its covering membrane it may lead to chronic lung failure. This discussion will be limited to diseases that involve the bronchi, the lung parenchyma and the pleura.

Table I

Essential Links in the Chain Necessary to Initiate and Complete a Single Normal Respiration

Functioning respiratory center.
Intact nerve supply to lungs, diaphragm, and chest wall.
Intact thoracic cage.
Patent air passages.
Normal intrapleural pressures with an elastic pleura.
Normal lung elasticity and volume.
Permeable alveolar membrane.
Adequate circulation of normal blood.

The purpose of the lungs is to provide for the exchange of oxygen and carbon dioxide between the blood in the pulmonary capillaries and the external air. Lung failure is present whenever they are so diseased as to be unable to carry out this function well enough to meet the normal needs of the individual. The usual causes of lung failure:

Pulmonary emphysema.
Pulmonary fibrosis.
Cystic disease of the lung.
Bronchial distortions and obstructions.
Chronic pleurisy.
Obstruction to the pulmonary circulation.

These will be discussed briefly.

Overinflation and distention of the alveoli is known as emphysema[2]. There are three types:

Compensatory or *complimentary emphysema* is associated with localized areas of loss of lung volume or bronchial obstruction. If the cause is removed the changes may be reversible.

Chronic hypertrophic emphysema is characterized by loss of elastic tissue from the lungs and destruction of the walls between the alveoli. These changes are irreversible.

Senile or *atrophic emphysema* occurs in old people and usually does not lead to severe symptoms.

Chronic hypertrophic emphysema is a frequent cause of lung failure. Its etiology is not well understood; it frequently follows one or more of the following:

Long-standing asthma.
Repeated or chronic bronchial and lung infections.
Pulmonary fibrosis secondary to irritant gases or dusts.
Chest deformities.
Localized loss of lung tissue.

Occasionally a relatively young man will be found with disabling emphysema that seemed to follow an acute virus infection of the lungs.

The cardinal symptom of emphysema is exertional dyspnea. Cough, wheezing and mucoid or purulent sputum are common. Cyanosis may be present in

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*Read before the annual meeting of the Medical Society of Virginia, at Roanoke, October 8-11, 1950.

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advanced cases. Examination shows the chest held in a position of inspiration. There is increase in the AP diameter, increase in dorsal kyphosis, prominent clavicles, and minimal motion of the chest wall with respiration: the so-called barrel chest. The accessory respiratory muscles are often used. There is increased resonance to percussion with decrease of cardiac dullness and depression of the area of liver dullness. The diaphragm is depressed and its motion is limited. The breath sounds are soft, distant, and expiration is prolonged. Wheezes and rhonchi are often present. X-ray examination can not accurately determine the degree of impairment of lung function. Films are likely to show a small, midline heart, decrease in normal lung markings interspersed with areas of fibrosis, and flattening of the diaphragm. Bullae or blebs may be present. On fluoroscopy, motion of the diaphragm is limited and slow.

The vital capacity is nearly always reduced. In addition, the time required for a complete expiration is markedly prolonged. The vital capacity can usually be increased and the expiration time decreased by the use of broncho-dilators such as adrenalin, ephedrine, aminophyllin, or atropine. Lung function studies show increase in residual air as well as poor distribution of the tidal air[3].

Pulmonary fibrosis is also common. When extensive, it leads to disabling dyspnea. It may lead to emphysema. When it is localized to a small area of lung it is not important and does not produce symptoms.

The fibrosis or scarring is caused by a number of agents. Common ones are:

Inhalation of dusts containing silica, asbestos, beryllium, etc.
Excessive X-ray exposure.
Pressure from intrathoracic tumors, cysts, or pleural effusion.
Repeated acute infections.
Chronic diseases, such as fungus infections, tuberculosis, or bronchiectasis.

The symptoms of pulmonary fibrosis do not differ from those of emphysema. Dyspnea, cough, sputum and wheezing are common. Cyanosis occurs late. Extensive fibrosis as shown by X-ray may produce no symptoms.

When fibrosis is advanced, examination shows a small and relatively immobile chest. It may be asymmetrical. The heart may be displaced if one side is involved more than the other. Chronic infection in the nose, throat or sinuses is common. X-ray films may show extensive areas of increased density. There are usually adhesions to the diaphragm. Fluoroscopy shows poor motion of the diaphragm. Laboratory studies may show tubercle bacilli, fungi, or various other bacteria. Vital capacity is reduced. There may be a prolonged expiration time. Lung function studies show that the vital capacity and maximal breathing capacity are usually reduced. The residual air is not increased in contrast to emphysema[4].

Lung cysts may be multiple or single. They may be congenital or acquired. When single, small and uninfected, they usually cause no symptoms. If large and multiple, they may cause complete disability. One would expect the symptoms to be variable. This is so. Cough, dyspnea, cyanosis, repeated respiratory infections, mucoid or purulent sputum, recurrent pneumonia, clubbed fingers and hemoptysis should make one think of cystic disease. The diagnosis can only be made adequately by X-ray examination.

Chronic bronchial or tracheal stenosis occur occasionally. Common causes are: scarring from old infections or trauma, tumors within or outside the lumen of the tracheo-bronchial tree, aneurysm, foreign body, or enlarged nodes. The lung scarring and contracture that follows chronic lung infection such as tuberculosis or abscess may cause bronchial distortion and stenosis. The stenosis is likely to cause atelectasis, lung suppuration or wheezing. The wheezing may be localized at the site of the stenosis or it may be diffuse due to widespread reflex bronchospasm. In either case dyspnea may be great. Cough is often very annoying and productive of mucoid, purulent or blood-streaked sputum.

The thickened pleura from chronic pleurisy may almost immobilize a portion of the lung. If it is extensive and bilateral, severe dyspnea will result. There may be no symptoms. The diagnosis can be made from a history of old pleurisy and from the X-ray findings. X-ray films may show minimal changes even in the presence of severe disease.

Chronic pulmonary hypertension due to disease of the pulmonary arteries occurs occasionally. It may be due to congenital abnormalities, pulmonary arteriosclerosis, multiple emboli or thrombi, aneu-

rysm or endarteritis obliterans of the smaller pulmonary arteries[5]. Symptoms are dyspnea, cyanosis and eventually right-sided heart failure. Pulmonary artery disease is usually not diagnosed clinically and is found as a surprise at autopsy. One should suspect it in the presence of a loud pulmonic second sound; physical, X-ray or electrocardiographic evidence of right ventricular hypertrophy; unexplained right heart failure; dilated pulmonary vessels seen in chest X-rays.

There are many causes of dyspnea. It is unusual for lung failure to be confused with central nervous system lesions, chest injuries, anemia, acidosis, obesity, hyperthyroidism, etc. However, it is commonly confused with heart failure and chronic asthma. At times it is very difficult to make a correct diagnosis. The correct diagnosis can usually be reached by careful history, and other examinations used for the diagnosis of chronic infections and allergy of the respiratory tract and cardiovascular disease. When available, lung function studies are of great value.

The problem of differential diagnosis is further complicated by the fact that lung failure not uncommonly occurs with either heart failure or chronic asthma. Occasionally all three occur together. When they occur together, each should be recognized and treated.

Characteristics that aid in differentiating heart failure and asthma from lung failure are listed in Tables II and III.

The diseases that usually cause lung failure are chronic, progressive, and potentially disabling. Each has irreversible structural changes. They are rarely cured. However, if improvement rather than cure is a worthwhile goal, a great deal can be accomplished. A slight increase in lung function may convert a coughing, wheezing and totally disabled man to one who can make a living at a sedentary occupation. If we are justified in strenuous efforts to treat such diseases as leukemia, inoperable cancer and chronic heart failure, we are certainly justified in making just as strenuous efforts to treat chronic pulmonary disease. The efforts may be more rewarding.

Adequate treatment of lung failure is dependent on the recognition and correction whenever possible of all factors affecting each patient. Thorough study will occasionally reveal a lesion such as a solitary cyst or bronchial stenosis that can be removed surgically. This should certainly be done. Most patients with chronic dyspnea will not be benefited by surgery.

Table II

Characteristics that Aid in Differentiating Heart Failure from Lung Failure

Heart Failure	Lung Failure
History of hypertension, rheumatic fever, syphilis or other causes of heart disease.	History of repeated respiratory infections, chronic asthma or pneumoconiosis.
Common symptoms are: edema, orthopnea, palpitation, exertional dyspnea, cough, abdominal discomfort, angina.	Common symptoms are: exertional dyspnea, cough, sputum, wheezing.
Examination may show evidence of heart disease (hypertension, cardiac hypertrophy, murmurs, thrills, arrhythmias, arteriosclerosis, etc.) or heart failure (edema, basal rales, pleural effusion, ascites, large liver, elevated venous pressure, decreased vital capacity, etc.).	Examination may show barrel chest deformity, limited motion of chest on respiration, increased resonance, decreased or absent cardiac dullness, depressed liver, immobile diaphragm, wheezes, distant breath sounds, decreased vital capacity with prolonged expiration time.
X-ray may show enlarged or abnormal heart and aorta shadow.	X-ray may show fibrosis, emphysema, cysts, or other lung disease. Heart is often small, low and in midline. Diaphragm moves poorly.
EKG may be normal or show evidence of any heart disease.	EKG may be normal or show a combination of any of these patterns: 1. Right heart strain. 2. P is small in I, tall, peaked and unnotched in II and III and inverted in chest leads. 3. Low voltage.[9]
Responds to digitalis, diuretics, and salt restriction.	Responds to bronchodilator drugs and control of infection.

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TABLE III

CHARACTERISTICS THAT AID IN DIFFERENTIATING UNCOMPLICATED BRONCHIAL ASTHMA FROM PULMONARY FIBROSIS AND EMPHYSEMA

Bronchial Asthma	Fibrosis and Emphysema
Usually begins at early age.	Usually follows years of asthma, repeated respiratory infections, or pneumoconiosis.
Usually occurs with other allergic phenomena.	Often occurs without evidence of allergy.
Frequently precipitated by known contacts.	Precipitating causes usually not recognized.
Characterized by periods of complete remission.	Exertional dyspnea is constant.
Dyspnea may occur at rest.	Dyspnea at rest is unusual.
Examination shows wheezing. Hay fever or respiratory infection may be present.	Examination shows emphysema or no physical abnormalities.
X-ray normal.	X-ray shows characteristic changes of fibrosis or emphysema.
Vital capacity normal between attacks.	Vital capacity always reduced.
Prompt relief from adrenalin or other drugs.	Slow and incomplete response to all treatment.

The real hope for people with chronic lung failure lies in the fact that there is an element of infection or bronchospasm or perhaps both in most of them. Their ability to breath can be increased by controlling the infection and spasm, but little can be done to alter existing degenerative changes.

Infection can nearly always be controlled at least temporarily. It may be in the sinuses, the pharynx, or the bronchi. Wherever it is, all infecting bacteria should be identified. The identity of the bacteria is becoming increasingly important as more and more antibiotics are developed. We have to know which bacteria are present and which antibiotics are most likely to control them. It would be a mistake, for example, to treat an influenza bacillus infection with penicillin when Terramycin would be so much more effective.

When infection is present, identify the bacteria and give the appropriate antibiotic in full doses for an adequate period of time. Most of the antibiotics can be given by aerosol. This method should be used for most chronic bronchial infections. The drugs should be used for at least a week. Often a week is not sufficient.

Repeated cultures are necessary. The original culture will often show penicillin sensitive organisms such as streptococci or staphylococci. After a week of penicillin treatment if symptoms persist, another culture may show that these bacteria have been destroyed and that some of the gram negative organisms are now growing. If Streptomycin or Aureomycin is added, there is frequent dramatic improvement.

Surgical or mechanical procedures to promote drainage are also helpful. These include lavage of the antra, removal of nasal polyps and obstructions, postural drainage and bronchoscopy.

The bronchospasm which manifests itself as wheezing or frank asthma can usually be controlled. Here, too, it is important to know what is causing the asthma. Common causes are:

Sensitivity to such factors as dust, pollens or foods.
Sinus or bronchial infection.
A reflex arising from a nasal polyp or other focus of irritation.
Emotional tension.
Heart failure.

When the cause of the asthma can be identified, specific treatment should be started. Even when no specific cause can be identified, symptomatic relief may be great. Drugs such as ephedrine, aminophyllin and Isuprel relieve the smooth muscle spasm. Potassium iodide may loosen bronchial secretions so that they can be coughed up more readily.

Smoking is a severe non-specific irritant. Its importance cannot be stressed too much. All patients with chronic dyspnea or cough should stop smoking for a diagnostic period at least. Many of them will get surprising relief.

Chronic lung failure does not exclude heart failure. Chronic lung disease is frequently complicated by *cor pulmonale* and right ventricular failure. In old

people, arteriosclerotic and hypertensive heart disease may also be present. Whatever the cause of the heart failure, it should be treated by the use of digitalis, diuretics, salt restriction and other conventional methods. The treatment of the heart failure secondary to *cor pulmonale* is often disappointing but is certainly not hopeless[6].

Whatever the cause of lung failure, physical activity which causes dyspnea should be prohibited or minimized. Contact with irritating dusts and fumes and with silica should be avoided. Breathing exercises and abdominal binders are often recommended. We have found them disappointing.

Other more drastic forms of treatment are needed for the occasional severely ill patient. These include the administration of oxygen, venesection, aspiration of bronchial secretions by catheter or bronchoscope, decompression of a tension pneumothorax, and decompression of large cysts by a catheter and suction. Cysts that have an epithelial lining should be excised.[7]. We have tried pneumoperitoneum in a number of emphysematous patients. None of them thought it helpful enough to keep it up indefinitely. ACTH has been followed by marked improvement in a few acutely ill patients. Cortisone should be as helpful.

Recently Comroe, Bahnson and Coates[8] have called attention to the fact that the administration of oxygen to emphysematous patients may lead to carbon dioxide retention, coma and death. This danger should not be overlooked when administering oxygen to an emphysematous patient.

Patients with chronic lung failure often require more than one form of treatment. For example, it is not uncommon to find pulmonary emphysema, infectious bronchitis and dust asthma in one individual. Such a patient should reduce contact with dust and be treated with dust extracts. He should also use broncho-dilating drugs and the appropriate antibiotics. Control of symptoms is usually temporary. These people have a chronic progressive disease. They require prolonged treatment.

A great deal can be done in the prophylaxis of chronic disabling lung failure. Treat all acute respiratory infections until they are cured. When possible the duration of the infection should be shortened. Do not withhold indicated antibiotics for fear of producing sensitivity. If sensitivity should develop another drug could be used for subsequent infections. Follow all pneumonias until they are clear by X-ray. Some may require bronchoscopy. Make a strenuous effort to control chronic asthma. Diagnose and treat all chronic coughs. Remember that even after chronic symptoms have developed each acute episode of infection or asthma tends to add to the permanent damage. These acute episodes should be treated promptly and enthusiastically so as to save every possible piece of good lung tissue.

Summary

Chronic lung failure is common. It should be differentiated from heart failure and recognized when it complicates asthma.

Causes of chronic lung failure are: Pulmonary emphysema; pulmonary fibrosis; cystic disease of the lung; bronchial distortions and obstruction; chronic pleurisy; obstruction to the pulmonary circulation.

Careful, prolonged treatment designed to eliminate infection, relieve bronchospasm and control heart failure often leads to considerable improvement.

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Discussion

Dr. Alexander McCausland, Roanoke: I think Dr. Guerrant has given us a very clear presentation, which

should serve to help us formulate a better approach to these diseases. The diseases are well known to us, but the terminology which he has used is relatively infrequently employed. I think it is important that although we speak of heart failure, liver failure, or renal failure, we very rarely hear the term "lung failure". It is important because, as he has stated, the differentiation of these chronic lung diseases from asthma cannot be overemphasized. That is because many of them masquerade as asthma, whereas the wheezing and other symptoms are due to chronic lung failure.

I think it is important also that Dr. Guerrant has pointed out the fact that occasionally we see a young individual with no previous evidence of pulmonary disease or asthma who has rapidly progressing emphysema; and, as best we can learn from the history, it all began with an acute virus infection of the lung.

The identification initially of the bacterial flora and the follow-up are extremely important. Dr. Guerrant has emphasized the need for identifying the bacterial flora before and after antibiotics have been instituted. Where possible, tests of the sensitivity of the bacteria to the different antibiotics should also be carried out in order that the most effective antibiotic agent may be used.

One should have a clear concept of the limitations of what can be accomplished by treatment. These lung changes for the most part are irreversible, and we cannot accomplish cure. That, however, does not justify an attitude of neglecting further treatment. These patients have a very small margin of pulmonary reserve. They operate on a very narrow margin between their maximum respiratory capacity and acute distress; and we should recognize that various conditions such as infections, emotional stress, exertion and allergy may encroach on and further reduce that margin and bring on severe respiratory distress. On the other hand, broncho-dilating drugs may increase this margin of pulmonary reserve. It therefore becomes necessary that we direct our efforts to preserving this margin by treating promptly and adequately infection and allergy and administer broncho-dilating drugs as needed rather than to try hopelessly for cure.

Very often you can discuss this matter very frankly with the patients, just as you do with diabetic patients, explaining to them that they have to live within certain limits. Once this is accomplished management is much easier.

I would like to say a word or two about the CO_2 combining power in these patients. Patients with emphysema frequently have a high CO_2 combining power. Actually what has happened over a long period of time is that they do not excrete CO_2 properly (because of inadequate ventilative function) and since it is an acid in the blood and reacts with sodium to make sodium bicarbonate which is actually what is measured in a CO_2 combining power. The CO_2 accumulation is so slow that the normal $\frac{H2C03}{NAHCO3} \frac{1}{20}$ ratio is not disturbed. The acidosis is compensated. The pH is practically normal. If, however, there is a sudden onset of emphysema or a sudden worsening of it, as with intercurrent pneumonia, etc., the CO_2 accumulates more quickly. Since CO_2 acts as an acid in the blood before it can react with sodium to form sodium bicarbonate the normal $\frac{H2C03}{NAHC03} \frac{1}{20}$ ratio will be disturbed. Thereby the acidosis becomes uncompensated. The pH will be lowered or on the acid side, even though the CO_2 combining power is high and makes one think of alkalosis. It is in these conditions that we need a blood pH determination.

As you know, the chemoreceptors are a highly specialized group of cells located in the carotid and aortic bodies. The reflex response of these chemoreceptors to hypoxia is of importance therapeutically. They are very resistant to minimal changes in pH and oxygen. The chemoreflex is highly resistant to hypoxia. Hypoxia, on the other hand, appears to be insufficient as a stimulus to the respiratory center. As a matter of fact, depression of the respiratory center is the predominating effect of oxygen lack. Quite often these patients carry on their respiratory function solely through this chemoreceptor reflex that is being stimulated by the hypoxia. The chemoreflex retains its viability and continues to exert influence on the respiratory center, which would otherwise be unresponsive to the body's emergency. It has been described as "a more primitive type of respiratory control which acts as a last line of defense against respiratory failure, capable of sampling the pH and oxygen content of the blood and signaling a message to the respiratory center when the tissues are threatened with a dangerous degree of hypoxia".

The patient with advanced emphysema maintains an arterial CO_2 far higher than normal, and since the accumulation of CO_2 is slow, the respiratory center becomes adjusted to this high level of CO_2. When this occurs the CO_2 no longer acts as an adequate stimulus on the respiratory center (CO_2 narcosis), and the respiratory drive arises in the chemoreceptors which are stimulated by the hypoxia (secondary to underventilation).

If we give these patients an over-dose of oxygen, what happens is that we remove the hypoxia which is actually keeping the respiration going, and changes such as delirium or coma and even death may follow the administration of oxygen. Recently a very good article by Dr. Comroe and his associates described this. They describe the various criteria by which one may predict in which patients we may expect these changes. I shall not go into these, but should like to say a word about the management of giving oxygen to these patients.

When we have a patient in distress, seemingly needing oxygen, how are we going to approach the problem? Certainly any approach from our present knowledge has to be empiric. Dr. Barach suggests beginning initially in these patients with a low concentration of oxygen, about 30 per cent. Use a nasal catheter giving about one liter per minute, increasing it every two or three days by one liter per minute until you reach seven liters per minute

and then switch to an oxygen tent. In this way, although the arterial CO_2 concentration may arise, the pH remains normal, and eventually higher elimination of CO_2 with each breath occurs. The arterial CO_2 is then decreased, and respiratory acidosis does not occur; whereas, if you give the patient an abrupt over-dose of oxygen, respiratory acidosis, delirium, and even death may ensue.

In the management of this condition the ventilative function should not be overlooked. The ventilative effort must be adequate to remove the CO_2 because in emphysema the greater increase in the residual air requires greater than normal tidal ventilation to maintain normal adveolar CO_2, and if increased ventilation is not forthcoming CO_2 level rises and CO_2 narcosis occurs. Electrostimulation of the phrenic nerve and artificial respiration may be used to increase ventilation.

Occasionally, we have a situation where we feel we have to give a patient a high concentration of oxygen immediately in order to combat severe degrees of anoxia. If so, it should be supplemented by artificial respiration to stimulate the ventilative function.

A word about CO_2-oxygen mixtures. Most commercial preparations are mixtures. The patient with respiratory failure does not suffer from the lack of CO_2; the CO_2 level is usually so high that given further CO_2 it may act as a depressant to the respiratory center.

The administration of drugs which are capable of depressing the respiratory center should be avoided.

The patient should be watched carefully for the first twelve hours after beginning the administration of oxygen. He should have a special nurse, who should be on the lookout for the beginning of the development of coma or any mental changes and anticipate the need for the administration of artificial respiration and have the means at hand for carrying it out should the need occur.

As to the broncho-dilating drugs that may be used, there is some indication that the use of Isuprel and similar preparations may be preferable to adrenalin, since they do not cause as much increase in the pulmonary blood pressure.

As to pneumoperitoneum, I certainly agree with Dr. Guerrant that I have seen no striking relief. Possibly the resting dyspnea is relieved a little bit, but that is an exceedingly hard thing to evaluate.

In closing, I should like to emphasize rehabilitation of these patients. These people have often worked at strenuous labor. Their respiratory function now will not allow them to return to that type of work. They are unemployed and are therefore unhappy, and the resulting emotional strain certainly has an effect in decreasing the small respiratory reserve which they have. So, if they can be trained to do some sedentary work within the limits of their small respiratory reserve, and can become employed, they are certainly happier patients and feel that they are gaining a little bit, and we have to depend on little things to keep them comfortable.

I enjoyed Dr. Guerrant's paper and wish to thank him for the privilege of discussing it.

Dr. John P. Williams, Richmond: I enjoyed Dr. Guerrant's paper and Dr. McCausland's discussion tremendously. Chronic progressive pulmonary failure is one of the most distressing and hopeless conditions with which we have to deal in the practice of medicine and is undoubtedly far more frequently a factor in breathlessness, especially in older people, than we have heretofore recognized, since the custom has been to attribute it all to myocardial degeneration.

Since the changes which cause chronic pulmonary failure are usually irreversible, no treatment yet devised can claim more than symptomatic or at most arrestive value. There are three things which we have come to rely on which we are convinced give these patients much comfort regardless of their effect on survival.

First, the creation and maintenance of an artificial polycythemia, if it is not already present, by the use of transfusions, iron and the therapeutic agents such as vitamin B_{12} which are stimulants to the hemopoetic system, and, finally, a diet rich in the foods which Whipple found most useful in the regeneration of blood. This is based on the common observation that the sthenic type with obesity, hypertension, and the florid face will invariably out-perform the asthenic type in spite of his puffing and blowing, and will almost invariably survive longer. They have compensated for a lowered oxygen tension by increasing the oxygen-carrying capacity and hence the total oxygen available to the tissues just as occurs in normal individuals who go to live at high altitudes.

Secondly, Dr. Guerrant has discussed the use of the antibiotics both as aerosols and parenterally. It is a common observation that decompensation in these patients is usually associated with inter-current respiratory infections. Furthermore, it is generally felt that these infections are responsible for the progression of fibrosis and the accompanying asthmatic bronchitis and cough for further destruction of lung tissue. In the early reports on Terramycin it was stated that it was selectively excreted into the bronchial tree by the bronchial mucosa. We have attempted to confirm this in our laboratory but have as yet been unable to do so because of the high content of tenacious mucus in the bronchial secretions. On the other hand, our clinical observations have convinced us that it is the most efficient of the group and we have toyed with the idea of keeping these patients on 500 mg. daily as prophylaxis just as sulfadiazine and penicillin have been used in an effort to prevent recurrences of rheumatic fever. We intend to continue our laboratory studies, using a liquifacient such as lysozyme, which should not affect the viability of micro-organisms.

Third, and last, there has appeared recently in the *Canadian Medical Journal* a preliminary report on the treatment of a case of pulmonary granulomatosis due to beryllium intoxication with ACTH with brilliant results. It would be entirely unreasonable to expect Cortisone, ACTH or any other drug to cause resolution of dense fibrous tissue already laid down, but we do know that it may be possible in some instances to prevent the formation of fibrous tissue by these agents. It is possible

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then that these agents may come to be used in conjunction with antibiotic therapy during acute infectious exacerbations, especially in young people. We have had one such case in whom the vital capacity, total ventilatory capacity and arterial oxygen saturation all increased significantly under such therapy coincident with considerable clinical improvement and return to a more or less sedentary occupation, but a much longer period of observation will be necessary and many more patients must be treated before conclusions are drawn.

DR. RENO PORTER, Richmond: I think this has been a very fine presentation, not only the original paper of Dr. Guerrant's, but the discussions that followed. We are coming to realize that chronic lung disease is quite prevalent. Many of these patients have been considered to have heart disease because of the respiratory distress, which is common to both conditions. Some of them have been treated fruitlessly for heart failure. I have in mind particularly a patient who had respiratory distress and was treated initially with digitalis because he was thought to be in heart failure. There was no particular improvement, and he was put on mercurials at increasing frequency. He still failed to improve as far as his shortness of breath was concerned and, in addition, because seriously ill with sodium depletion syndrome. He was brought into the hospital weak, with lowered blood pressure, and very little urinary output. The administration of saline, particularly hypertonic solutions, brought him out of his salt depletion state. Subsequent treatment of his chronic lung disease brought about improvement in his respiratory distress. This illustrates the importance of differentiation between these two conditions, since treatment of chronic lung disease with cardiac drugs does no good and may actually do harm.

Dr. Guerrant mentioned vital capacity, and, in this connection, I would like to emphasize the fact that vital capacity is not only a measure of volume, but also should be limited as to time. There are many patients with chronic pulmonary disease who can attain a vital capacity of 75 to 90 per cent if they are permitted to blow into the apparatus for as long as they can (5 to 8 seconds). This gives a falsely high value because actually their vital capacity may be only 30 to 50 per cent when they were limited to two seconds, which is time enough for a normal person to attain maximum capacity.

We have been impressed by the benefit which these patients derive from Hydryllin. This drug is a combination of diphenhydramine (a benadryl base) and aminophyllin. We studied this drug several years ago and found that it increased ventilatory capacity without apparent increase in respiratory work. This drug works particularly well in chronic lung disease, allowing the patients to undertake increased activity with less respiratory distress. It appears to be the drug of choice in the long-term treatment of the chronic condition, but not particularly of value in the acute flare-ups that may occur.

I want to thank the speaker for his most interesting paper. I think it is a very timely one for all of us.

DR. GUERRANT, closing the discussion: I should like to thank Dr. McCausland, Dr. Williams, and Dr. Porter for their remarks and to emphasize one or two other things.

Certainly the thing Dr. McCausland brought out is true. We are striving for improvement in these patients. We cannot cure them, but frequently we can do them a lot of good.

When you see a patient with emphysema in an oxygen tent and he begins to go into coma you had better take him out.

I have seen people improve under treatment with Terramycin after failing to improve on other antibiotics. I do not know about its selective secretion by the lungs.

I agree with Dr. Porter that Hydryllin is a very useful drug in these patients.

THE EVALUATION OF THE CARDIAC PATIENT*

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Advanced congestive heart failure is seldom difficult for the attending physician to recognize with certainty. There is usually the familiar picture of dyspnea and orthopnea associated with the congestive phenomena of venous distention, pulmonary rales, hepatomegaly and peripheral edema as well as various cardiac manifestations of dysfunction. For the patient with heart disease to live his maximal span efficiently, however, it is imperative for the physician to be able to recognize the earliest evidences of a weakened myocardium and institute proper therapy before dangerous gross failure occurs.

This recognition is of particular importance to the patient who is about to undergo some operative procedure, for, in spite of the improvements in anesthesiology as well as surgical techniques, the decompensated patient is still an extremely bad risk. Once the failure has been controlled, surgery can be carried out with far less danger. Time often does not allow the internist to follow a course of therapeutic trial or one of prolonged observation, though he would often like to, especially when faced with a patient showing the debilities of advancing years, or perhaps a younger individual with hypertension.

The early stages of failure are easily confused with other conditions which are not at all improved by cardiac medications and, indeed, at times may be made worse by them. For instance, the patient with chronic pulmonary disease may give a history of dyspnea and orthopnea similar in many respects to that found in heart failure, and rales at the lung bases may add to the confusion. In like manner the debilitated and obese patient may complain primarily of dyspnea and palpitation though there may be no weakness of the myocardium.

To establish the presence of heart failure the physician often must employ all of the various modes of investigation. A careful history should, among other things, bring out the duration of dyspnea and edema and the circumstances under which they occur. During the physical examination one should look for cyanosis, venous distention, changes in the lung fields, enlargement of the liver, and the type and location of edema if present. Careful attention should be given to the size of the heart and the character of the sounds as well as murmurs. X-ray and electrocardiographic studies are often necessary components of the investigation.

In general terms heart failure may be defined as that state in which the work required of the heart exceeds its functional capacity. In severe heart disease this capacity or reserve is reduced to a point where ordinary activity cannot be tolerated. Where there is less severe heart disease, acute pulmonary edema may result from unaccustomed and strenuous activity. With the resulting congestive phenomena there is a diminution of renal output and an increase in blood volume. Failure is then perpetuated by this added circulatory load and death may ensue unless the demand on the heart is diminished by instituting rest, diuretics, oxygen, digitalis and other measures to restore a proper ratio between demand and capacity.

When heart failure is present, the most important signs to appear are gallop rhythm, pulsus alternans and venous hypertension. Those signs of lesser importance, such as tachycardia, hyperpnea, pulmonary rales, accentuated pulmonary second sound, hepatomegaly, and edema, though almost always present, are more difficult to evaluate since they occur frequently in the absence of heart disease.

We use the term gallop rhythm to refer to the diastolic occurrence of a third heart sound. This, contrary to a systolic gallop rhythm, is indicative of serious heart disease except in rare instances as prolongation of A-V conduction.[1] Its mechanism is poorly understood, but it is not often heard at rates below 90, and at times with tachycardia there is a summation of an early and a later or presystolic impulse giving rise to a loud third sound.[2] For these reasons, perhaps, there has been a tendency to emphasize the rate of the heart in the pathogenesis of gallop rhythm rather than the inadequacy of the heart for the load placed upon it causing

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that accelerated rate. Nevertheless, if the physician becomes aware of the possible disparity between the load and reserve power of the heart, he will realize that he cannot be content with the absence of a gallop rhythm in a patient suspected of having a weakened myocardium when that patient has been at rest for some time. It is logical to assume that there is an immense difference between the cardiac status of a patient who has just climbed two flights of steps and of the same patient after he has been near basal conditions for an hour or two.

It is important therefore to be aware of these factors in interpreting a gallop rhythm. The physician will frequently be rewarded for his efforts in borderline cases if he listens carefully to the heart after having the patient exercise. In one who is convalescing from a myocardial infarction a gallop may appear after he has undressed and again be inaudible in a matter of minutes. In other cases more strenuous exercise is necessary.

One may be confused by the normal diastolic third heart sound which is so common in healthy children and young adults. It does indeed make the determination of a pathologic gallop rhythm almost impossible in these individuals, but this normal third sound is thought to disappear universally bv the age of 20, probably somewhat sooner. Reduplication of the second sound may also be the source of some concern, especially in the presence of tachycardia where the distinction may be impossible. At slower rates the reduplication or splitting will become obvious.

Of equal significance as a criterion of left ventricular weakness is pulsus alternans which occurs primarily in hypertensive and coronary heart disease. In spite of its importance this is one of the most neglected findings in medicine. It is rarely recorded on hospital charts, though in a series of 201 cases of cardiac decompensation White found it in a third,[3] an incidence equal to that of auricular fibrillation. Contrary to common belief, it is exceptional to detect pulsus alternans at the radial pulse by palpation. Instead it should be sought for with a sphygmomanometer, raising the cuff pressure above the systolic level and slowly lowering it until the first sounds are heard. When alternation is present only every other circulatory impulse is heard initially, the weaker impulse coming through as the pressure is reduced further. Where the difference is small (e.g. 4 mm. Hg.) time must be taken to be sure that the change is not from the normal respiratory variation.

Like gallop rhythm, pulsus alternans is inconstant and may be absent in the face of frank failure. It may be expected to diminish or disappear in the cardiac patient whose condition has been improved under treatment, or in the ambulatory patient who has been at rest. Conversely, in patients with diminished cardiac reserve, pulsus alternans may at times be produced by exercise, or, if the alternation is of minor degree, may be increased to 10 mm. Hg. or more.[4] Though this effect of exercise is quite transient, the value of the procedure is the demonstration of unequivocal evidence of a weakened myocardium.

The pathogenesis of this phenomenon is obscure but is undoubtedly related to incomplete recovery of the muscle fibers after each forceful contraction. It becomes accentuated for several beats following a ventricular extra-systole and is distinguished from bigeminal rhythm by the occurrence of the weaker impulse closer to the preceding strong beat in bigemini, whereas in pulsus alternans the weak beat is slightly closer to the succeeding beat.

The general state of venous pressure in patients with heart disease can be estimated in the office with some degree of accuracy without the use of a manometer. Gross distention of the neck veins with the patient in a sitting position is rarely overlooked. Where lesser degrees of venous hypertension are present, the abnormality can be detected by raising the head and chest from a reclining position to a point where the cervical veins are partially filled and pulsating. The pressure is probably abnormally high if the cervical veins pulsate or become distended when the thorax and head are at 45 degrees from the horizontal. Similarly, with the patient in the sitting position the height of the column of blood in the jugular vein above the third costal margin is noted. Normally, that is, with the pressure below 10 cm. the vein will not be evident. Above 25 cm. the vein is distended up to the ear.

Another important maneuver is the observation of venous pressure change during abdominal compression. Winsor and Burch[5] noted that while compression in *normal supine* subjects produced no change or a fall, in patients with mild congestive failure there was an appreciable rise amounting to average increase of 96 mm. With the patients in a sitting

position the change was less but still quite prominent. Cardiac patients without failure responded in a similar fashion to normals, and those with severe grades of failure with initial hypertension showed a further rise of pressure. It is important to note that in patients with ascites from causes other than heart failure, abdominal compression produced no increased venous pressure.

During exercise of the patient with diminished cardiac reserve there is an abrupt and sustained rise in venous pressure which returns slowly to the resting level after the exercise is completed. In subjects with normal hearts, on the other hand, moderate exercise produces a rise of a few cm. at the onset of exercise followed by a fall coming on after five or ten minutes of continued exertion. The extent of this fall may be such that the venous pressure has returned to its control or resting level while exercise is still in progress. On cessation of exercise the venous pressure drops immediately to the resting level or below.

The importance of the ventricular rate in auricular fibrillation also should be stressed. It is a mistake for the physician to be satisfied with a rate of 90 or less in a patient with this malady who has been confined to bed or who, though ambulatory, has been at rest for some time. Where digitalization is incomplete, light exertion will cause dyspnea and the ventricular rate, which at rest seemed quite normal, will quickly rise to 100 and above. In auricular fibrillation adequate digitalization should hold the ventricular response to 90 or less after light exercise, such as walking ten or fifteen paces, unless there is heart failure or mitral stenosis of a degree which with sinus rhythm would cause tachycardia. In the bed patient the absence of a pulse deficit cannot be relied upon unless the ventricular rate is maintained below 90 after the patient has been made at least to sit up and lie down two or three times.

In summary, we have stressed these objective evidences of heart failure since they are often early in their appearance and may be the only clues which the physician may have with which to establish his diagnosis. If either gallop rhythm or pulsus alternans is found, weakness of the myocardium is present. If they are absent at rest and failure is suspected but cannot be demonstrated conclusively, it is well to exercise the patient in the expectation of producing one or the other of these signs as the load on the heart exceeds its reserve strength. If they do not occur, ventricular weakness can by no means be ruled out. It is the presence of these signs rather than their absence that is important. The patient undergoing surgery can be evaluated much more accurately if observed during exercise than at basal state, and a differentiation between the debilities of heart disease and those of pulmonary disease can be established in a similar fashion. Finally, the physician may obtain some appreciation of the reserve strength of the heart by noting the amount of exercise necessary to produce these signs of a failing ventricle.

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Discussion

Dr. Reno R. Porter, Richmond: I am very happy to have the opportunity of opening the discussion of this very interesting paper by Dr. Williams. We know that the heart has a tremendous reserve capacity and that heart disease may exist without any particular disability. We recognize, therefore, that patients may have heart disease alone or with varying degrees of so-called "heart failure". The outlook for the patient varies, depending upon how much the myocardial reserve has been reduced.

In his paper, Dr. Williams has stressed the points that differentiate a patient who has heart disease and a competent myocardium from one who has a failing myocardium. These phenomena are present when the heart is under stress, namely, gallop rhythm, pulsus alternans, and a rising venous pressure. There are also certain other phenomena which represent the consequences of a retention of salt and water in the body, which now appears to be the result of compensatory mechanisms brought into play by previous episodes of true heart failure (inadequate output). These are the phenomena more generally associated with heart failure but actually representing chronic changes. The points which Dr. Williams has stressed represent acute phenomena and demonstrate latent myocardial failure which may or may not be associated with the chronic congestive failure mentioned. They indicate that the heart, while appearing to be competent, is actually on the borderline of compensation. This is important to know, since the presence or absence of

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these findings guides us in our treatment and prognosis.

I think Dr. Williams should be congratulated for bringing these points to our attention. I am particularly pleased that he emphasized the phenomena that occur on exertion because these are the most important signs in detecting early myocardial insufficiency. The patient otherwise may be very comfortable and present no other signs of impending disability.

I wish to thank Dr. Williams for the opportunity of discussing this paper which I consider a very important one.

DR. PAUL D. CAMP, Richmond: I enjoyed Dr. Williams' paper. I think his discussion is particularly important in that he brought out the important physical signs and findings for which we should look in this type of patient in trying to differentiate whether they are actually having failure, or whether it is borderline failure, or whether there is no embarrassment of the circulation present. I certainly agree with him on the findings of gallop rhythm and pulsus alternans. Incidentally, the first time I became interested in heart disease was when I was a fourth-year student working with Dr. Edwin Wood on pulsus altenans.

The prognosis in patients with pulsus alternans, as Dr. Williams indicated, is exceedingly guarded and poor. If I am not correct I should like to be corrected, but I think the general outlook in patients with pulsus alternans is that they will not live over eighteen months to two years at the longest, generally speaking.

I wish to commend, likewise, Dr. Williams' observations on gallop rhythm, particularly the slow rate and the fact that it may often be noted if the patient is made to exercise. For instance, when a patient gets up on the examining table we have noted that gallop rhythm has occurred. I think we should keep that in mind.

In patients with chronic pulmonary disease, for example emphysema, there is one test Dr. Williams indicated which I think is very helpful. If you have these patients in the office and have them do a simple exercise test, if the dyspnea is due to emphysema you will find that the pulse rate will not go up nearly as much as if the dyspnea is due to myocardial damage and failure, and, of course, the rate will return to normal much more quickly.

With regard to operation, of course, we are trying to decide whether these patients are suitable for operation at that time. I think if there is a real emergency we can take more of a chance than we should with elective operations. I believe that in elective operations we should be sure that the patient at least has a good chance of recovery, because oftentimes they can live for many years comfortably or with a little discomfort from the disease for which they are operated upon. The surgeons, of course, are more upset about the murmurs they find than we are; and we are more upset about the other things which we find.

The presence of aortic stenosis, as we all know, is not very favorable for operation or for other things. In fact, these patients are apt to drop out at almost any time.

I should like to mention one other thing in the evaluation of the cardiac patient which Dr. Williams did not cover because of the nature of his paper and because of the time. That is coronary insufficiency without any evidence of actual myocardial failure, or, I should probably say, evidence of congestive failure. I think it is important to inquire very carefully and take a very careful history in these patients to try to determine whether they do have coronary insufficiency, as indicated by the syndrome of angina pectoris or past history of coronary thrombosis or occlusion. I personally do not always find the determination of angina pectoris such an easy thing to make. I may just not know how to do it, but that is a fact. I think the most important thing is to inquire very carefully in regard to any discomfort—not necessarily pain but any discomfort—in the chest radiating to the arms or neck, which is brought on by exertion or excitement, and coming on under the same circumstances time and time again. I think that generally means angina pectoris, although of course it does not always mean that.

Again, I should like to congratulate Dr. Williams on his paper and for bringing to our attention the very important physical signs which he brought up.

DR. WILLIAMS, closing the discussion: I should like to thank the gentlemen who discussed the paper.

In regard to the prognosis of pulsus alternans, it has, generally speaking, a bad outlook. However, I would emphasize again that it is the circumstances under which the pulsus alternans occurs that are probably most important. If we have a patient who has been at rest and shows a severe degree of pulsus alternans, ten, fifteen or twenty mm. of mercury, his prognosis is much worse than that of the patient who would show pulsus alternans only after strenuous exercise.

EVALUATION OF CERTAIN NEW THERAPEUTIC MEASURES IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS*

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The research of Hench, Kendall and others on certain hormones from the hypophysis (ACTH) and adrenal cortex (Cortisone) and their effect on rheumatoid arthritis has prompted research into other related compounds in the hope that they could produce similar effects.

Lewin and Wassen,[1] in the November, 1949, *Lancet*, reported on their work in using combined injections of desoxycorticosterone acetate and ascorbic acid on rheumatoid arthritis. Their series comprised 9 patients (6 women and 3 men) with mild to severe rheumatic disease of the joints of two weeks to fifteen years' duration. The method described was to use intramuscular injections of 5 mg. of desoxycorticosterone acetate in oil immediately followed by an intravenous injection of 1 gm. ascorbic acid. They reported that within five minutes after the injection, the articular pain began to diminish and articular mobility began to increase. Fifteen to thirty minutes later pain practically disappeared and the mobility improved as much as the anatomical changes in the joints or muscular atrophy would allow. The report indicated that all the patients reacted in a similar way. This effect lasted from two to six hours and occasionally more than twenty-four hours. They also reported that in one or more acute cases, one or two injections have been enough to banish the pain for two or three weeks. Shortly after this, LeVay and Loxton[2] treated 80 cases of rheumatoid arthritis in the same manner and reproduced the same results reported by Lewin and Wassen[1]. There have been several reports by other investigators of a similar favorable response.

Curre and Will[3], however, in their investigation were not convinced that desoxycorticosterone acetate and vitamin C were of any value in the treatment of rheumatoid arthritis. Others have agreed with these later workers. An editorial in the May 27, 1950, *Lancet* stated that no substance except Cortisone and ACTH can be held to have contributed to the endocrine treatment of rheumatism. In their opinion it was difficult to see how the intramuscular injections of a very small quantity of hormone in oily solution could be responsible for any substantial changes in rheumatoid arthritis within a few minutes. Cortisone and ACTH can remove symptoms but the improvement seems to take much longer than the five to fifteen minutes claimed for desoxycorticosterone. Moreover, the quantities of Cortisone needed are much greater than the quantities of desoxycorticosterone which have been used. Even if some theoretical mechanism could be devised for the conversion of desoxycortone into Cortisone, it is not clear why 5 mg. of the former should have an effect comparable to more than 100 mg. of the latter. Desoxycortone and ascorbic acid therapy came in for further condemnation from E. C. Kendall and Philip Hench at the National Academy of Sciences in 1950. They stated at this time that a number of other compounds related to Cortisone were without effect.

In rheumatoid arthritis, spontaneous remissions are common. These are usually subjective and are of very variable duration, lasting from a few hours to several months or years. Most patients say they have good days and bad days, associated with changes in the weather. Also, the results of treatment with any specific drug are influenced by the personality of the patient, and the patient's performance is limited not only by the damage to and the pain in affected joints, but also by his or her willingness to move the joints. Thus the power of sug-

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gestion on any patient has to be taken into consideration in giving any drug.

EFFECTS OF DESOXYCORTICOSTERONE ACETATE WITH ASCORBIC ACID IN RHEUMATOID ARTHRITIS.

In our study ten patients with rheumatoid arthritis were treated daily by the intramuscular injection of 5 mg. desoxycorticosterone acetate followed immediately by the intravenous injection of 1,000 mg. ascorbic acid, for a period of at least two weeks. All the patients were suffering from active disease and had been under observation for periods of months to years. The disability ranged from Stage II to Stage IV, Class II to Class IV as defined by the Committee on Therapeutic Criteria of the American Rheumatism Association.

RESULTS

1. *Clinical.*—Four of the ten patients reported transient relief of pain and increased mobility of joints lasting from a few minutes to a few hours following the first injection. Two stated that they felt worse after the first injection and the remaining four stated that there was no change. The injections were carried out on all of the patients for 14 days. In the four patients reporting relief on the initial injection, we were unable to duplicate this result by later daily administration. In the remaining six patients, further daily injection also failed to give improvement. At no time in any patient were we able to demonstrate any objective improvement in swelling or mobility.

2. *Laboratory:*

Sedimentation Rate.—Daily sedimentation rates (Westergren) were done in the majority of the cases and three times weekly in others. No significant drop in sedimentation rate was observed in any of the patients.

Eosinophil Counts.—Eosinophil counts were carried out daily on four of the patients. There was no drop in total circulating eosinophils and no rise following cessation of therapy.

EFFECTS OF DELTA 5 PREGNENOLONE IN RHEUMATOID ARTHRITIS

Pregnenolone (Delta 5-pregnen-3 beta-01-20-one, melting point 190 C) was first obtained synthetically from stigmasterol by oxidation of the C 20 side chain[4] and subsequently from cholesterol by the same method[5]. It has been isolated in small amounts from hog testes[6], but its isolation from human sources has not been reported.

Its relation to the physiologically important steroids in chemical structure and in pharmacologic properties has given rise to speculations about its possible role in the human organism as an intermediate substance in the synthesis and metabolism of these steroids[7].

While chemically it can be regarded as a direct oxidation product of cholesterol, it can in turn be transformed to dehydroisoandrosterone by oxidation at C 17, to progesterone by oxidation at C 3 and to desoxycorticosterone by oxidation at both C 3 and C 21[8].

The resting adrenal cortex is rich in cholesterol esters which are depleted when the experimental animal is subjected to stress or when the adrenal cortex is stimulated by injection of adrenocorticotropic hormone. There is therefore good evidence that cholesterol is utilized in the synthesis of the steroid hormones, and the pathway of this synthesis may well be through pregnenolone.

Pharmacologically it displays to some extent all the hormonal activities common to the naturally occurring steroids, as shown in animal experiments. It was used extensively by Hoagland[9] and by Pin-

TABLE I

RESULTS OF TREATMENT OF RHEUMATOID ARTHRITIS WITH DESOXYCORTICOSTERONE ACETATE WITH ASCORBIC ACID

Number of Cases	Stage	Class	Duration of Treatment	Initial Clinical Results	Final Clinical Results (2 weeks)	Sed. Rate	Eosinophil Count
4	II	II	2 weeks	Good	No change	No change	
4	III	III	2 weeks	No change	No change	No change	No change
2	IV	IV	2 weeks	Worse	No change	No change	

cus[10] to reduce increased ketosteroid excretion which occurs as the result of stress in aviators. Simultaneously with the reduction of the ketosteroid excretion, the psychomotor performance improved. Hoagland postulated that its administration creates an optimum steroid balance, though the mechanism of conversion is obscure. While these observations were made on essentially healthy persons, pregnenolone will also reduce the excessive ketosteroid excretion of pathologic origin which occurs in virilism in women[11].

It appears to be free from toxic effects in man when administered in relatively large doses. Carbohydrate and electrolyte metabolism is unaltered even with prolonged administration, and no effect on renal clearances was observed by Abels and his associates[12].

In our study ten patients with active rheumatoid arthritis were treated daily with injection of 300 mg. pregnenolone. All the patients were suffering from active disease and their disability ranged from Stage II to Stage IV, Class II to Class IV as defined by the American Rheumatism Association.

Here, again, a careful attempt was made to assess pain, stiffness, swelling, tenderness, range of motion, etc., before, during and following treatment.

Results

1. *Clinical.*—One patient was treated daily for 23 days without any objective or subjective improvement; one was treated for 28 days with the same negative results; five were treated for 30 days with no results; two were treated for 36 days with no improvement. One patient claimed subjective improvement during early treatment and was kept on therapy for 60 days. However, during the latter part of treatment even subjective improvement was denied and treatment was discontinued after 60 days.

2. *Laboratory:*

Sedimentation Rate.—Sedimentation rate (Westergren) was done bi-weekly. No significant changes were noted.

Eosinophil Counts.—Eosinophil response counts were carried out before treatment and approximately two weeks after treatment. There was no significant change.

Effects of Cortisone in Rheumatoid Arthritis

In contrast to our completely negative results with these two drugs, we would like to report briefly on our results in the treatment of our first ten cases of rheumatoid arthritis with Cortisone.

After preliminary studies, treatment with Cortisone followed a fairly set pattern modified slightly to meet varying clinical situations and the variable responses of the individuals. During the first twenty-four hours 300 mg. of Cortisone was given in a dosage schedule of 100 mg. every eight hours. During the second twenty-four hours and occasionally extending over a period of from twenty-four to seventy-two hours, 200 mg. a day in a dosage schedule of 100 mg. every twelve hours. For the next seven days the dose was fixed at 100 mg. a day given in a single dose. Following this, the dose was reduced by 25 mg. stages, usually every second to third day, first to 75 then to 50 and occasionally to 25 mg. daily. At the time of discharge from the hospital, the patient's maintenance dose was usually set at from 25 to 75 mg. per day[13].

Evaluation of Results

Excellent.—Two cases were considered to have had excellent results. They were completely relieved of resting pain, and joint and muscle stiffness. Joint

Table II

Results of Treatment of Rheumatoid Arthritis with Delta 5 Pregnenolone

Number of Cases	Stage	Class	Duration of Treatment	Initial Clinical Results	Final Clinical Results	Sed. Rate	Eosinophil Count
1	III	III	23 days	No change	No change	No change	No change
1	III	III	28 days	No change	No change	No change	No change
5	II	II	30 days	No change	No change	No change	No change
2	III	III	36 days	No change	No change	No change	No change
1	IV	IV	60 days	Good	No change	No change	No change

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swelling and deformities were completely controlled and the patients developed motion pain only after extreme exertion. The maintenance dose of Cortisone in one patient was 25 mg. per day and in the other 25 to 50 mg. per day with intervals as long as three weeks without treatment or return of symptoms. Both of these cases had had the disease less than two years. (Fig. 1)

however, was present on moderate exertion, and they still showed residual joint swelling and moderate joint deformities. The maintenance dose of Cortisone varied between 50 and 75 mg. per day, although one patient in the group had a remission for two weeks after discontinuing therapy. The duration of the disease in this group extended from two to ten years. (Fig 2)

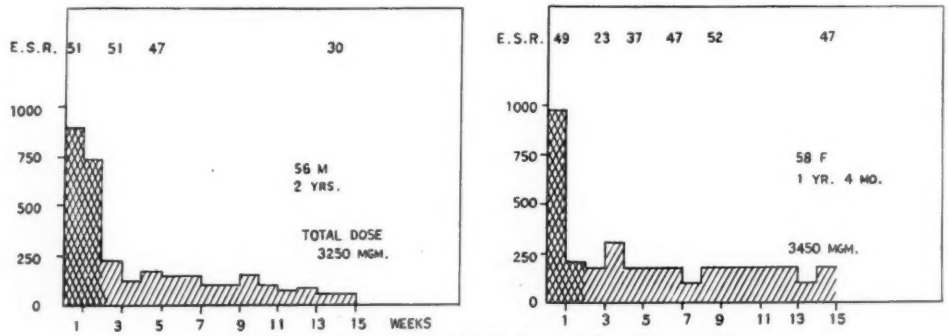
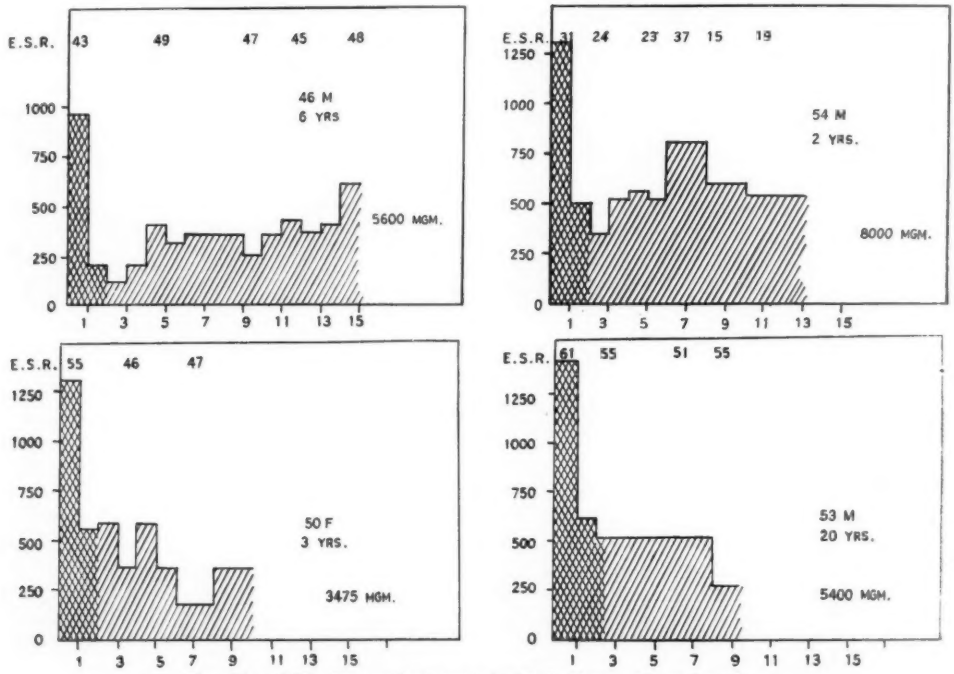


Fig. 1. Two patients treated with Cortisone with excellent results.

Good.—Four patients were considered to have had good results. In these patients resting pain was completely relieved and there had been a marked improvement in muscle and joint stiffness. Motion pain,

Fair.—Two cases were considered to have had only fair results. In these two cases resting pain was under good control, but they experienced only moderate relief of muscle and joint stiffness, motion pain



Figs. 2A and 2B. Four patients treated with Cortisone with good results.

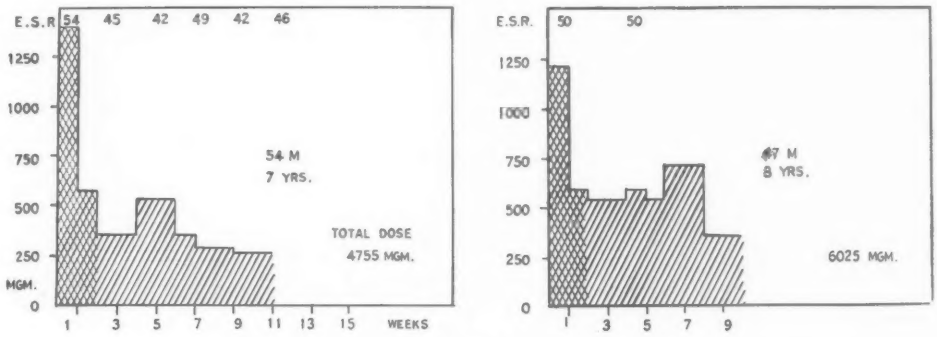


Fig. 3. Two patients treated with Cortisone with fair results.

returned after slight activity, and the patients' actions were markedly restricted due to persisting severe deformities. The disease in each had existed from five to twelve years. The maintenance dose of Cortisone varied between 50 and 100 mg. per day. (Fig. 3)

Poor.—The results in two cases were considered poor and in both treatment with Cortisone had to be discontinued. In one of these cases a persistent leukopenia and granulocytopenia developed, and all the signs and symptoms of the disease recurred after the drug had been discontinued. In the second case very large doses of Cortisone, in excess of 100 mg. per day, were necessary to keep even resting pain under control, the patient developed an abscess at the site of injection, and in addition became very apprehensive and anxious about the development of toxic side effects. She also showed a marked accentuation of her arthritic complaints after injections of Cortisone when the dose was below the adequate maintenance level. The disease in both of these patients had existed from ten to twenty years and both showed severe deformities as a result of the disease. (Fig. 4)

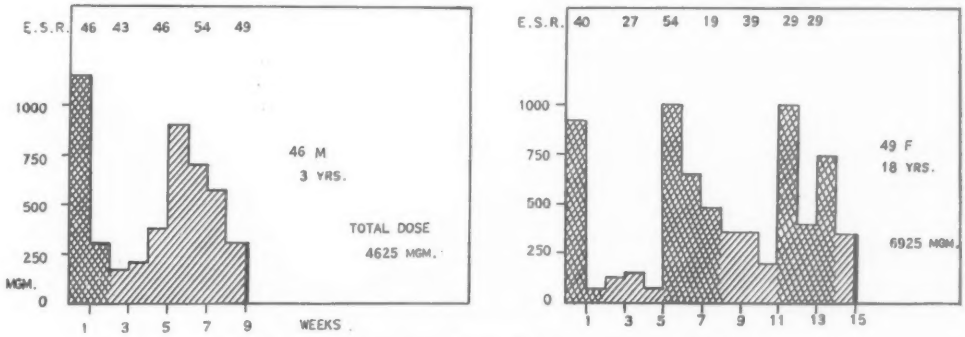


Fig. 4. Two patients treated with Cortisone with poor results.

SUMMARY

In summary, we do not believe that either the use of desoxycorticosterone acetate with ascorbic acid or the use of pregnenolone has any beneficial effect in the treatment of rheumatoid arthritis. In contrast, Cortisone often shows dramatic beneficial effects and these effects are maintained in many cases kept on maintenance doses in our series of cases.

The brand of desoxycorticosterone used in this investigation was Percorten first and later Percorten-Sodium ascorbate emulsion very kindly furnished us by the Ciba Pharmaceutical Products, Inc.

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DISCUSSION

DR. JOHN P. WILLIAMS, Richmond: When we started this work with DOCA and Pregnenolone, Cortisone was not available to us and the frantic search was on for some physiologically active, more easily available and less costly therapeutic agent among the other steroid compounds. The early reports on both of these drugs had been encouraging to say the least and we were very anxious to confirm these results and to help these hopeless sufferers. There is no use in wasting time by discussing the details of this study since Dr. Wingfield has covered it so clearly and thoroughly; suffice it to say that we could not convince ourselves that we caused significant improvement in a single case of rheumatoid arthritis.

There is one case which should be mentioned which was not included in this report because he did not have rheumatoid arthritis. He was a middle-aged negro with sarcoidosis accompanied by multiple lesions of the bones with extreme deformity of both hands resembling those seen in the textbook illustrations of leprosy. During the uneventful course of his hospitalization, he became acutely ill with a red throat, temperature of 102°, and very severe arthritic symptoms involving many joints but especially the badly damaged hands. He was started on penicillin first with little immediate improvement. Two days later DOCA and ascorbic acid were added to the therapy and improvement followed immediately with disappearance of fever and acute arthritic symptoms in 48 hours. You may take this observation for what it is worth, always remembering that "*post hoc, ergo propter hoc*" is one of the most notorious of logical fallacies.

One of the phases of this situation which has always fascinated me is the fact that our literature will so frequently and almost simultaneously report diametrically opposed observations. In this instance, how is it possible for a group of observers just as honest as ourselves to obtain improvement in a high percentage of cases when we fail utterly? Or to carry this inquiry a little further, how is it possible for an intelligent and experienced observer to accept improvement which occurs within 5 minutes of administration of any agent, save on a functional rather than an organic basis? The answer will have to deal both with the patient and the observer. The former has been covered recently by Dr. Harold Wolff, Dr. Stewart Wolf, *et al.*, in the *American Journal of Clinical Investigation* under the title, "The Pharmacology of Placebos", in which they show that inert substances plus suggestion will in many instances call forth a greater physiological response than physiologically active substances without suggestion. The rest of this question could probably be answered if these gentlemen would report a study on "The Psychology of the Ardently Wishful Observer".

Dr. Wingfield has also reported our results with Cortisone since it has become available, for contrast with the lack of results with the other agents. I do not believe that we have stressed sufficiently the undesirable side-effects of this therapy. We have noted the development of the "moon-face", acne and transient dependent edema even when electrolyte values were normal, but these have been easily controlled and no deterrent to continuation of therapy when indicated. We have not seen significant hypertension or any diabetic tendency. In our series we have noted two psychotic reactions which were sufficiently severe to require locked ward care. Both of these recovered completely. One other patient, nearly blind from sarcoidosis with bilateral uveitis, became first euphoric, then agitated and confused and left the hospital against medical advice since he was not thought to be sufficiently disturbed for commitment. He also recovered completely and returned later, no improvement in vision having resulted. All of these patients were being treated for conditions other than rheumatoid arthritis and are not included here.

One of the most distressing if not the most dangerous of the side-effects of Cortisone therapy is the marked exaggeration of despondency and hopelessness which supervenes with the rapid relapses following cessation of therapy. Patients who have established equanimity in spite of the burden of pain and incapacity which they bear, see their hopes and aspirations soar to unprecedented heights with the exhibition of the "miracle drug" and abetted by the customary euphoria, to be dashed precipitately when they return to a condition which may actually be or merely seem to be worse than before therapy. We are becoming more and more forcibly impressed with the necessity for using sound judgment in selection of cases for treatment.

DR. OSCAR SWINEFORD, Charlottesville: We have tried DOCA and ascorbic acid with essentially the same results as reported. We have noticed very striking subjective improvement that lasted for a matter of an hour or two in a few patients, but we have never found any lasting improvement, nor have we been able to repeat the transient result first obtained.

We, too, have had difficulty with ACTH and Cortisone, with acute mania once, development of hypertension and acute failure once, and troublesome depression in an-

other instance. In several instances a mild diabetic tendency has been accentuated. We have had pigmentation of the skin in the form of freckling, moon face, transient edema in several instances. None of the consequences of ACTH and Cortisone administration persisted more than a few days after the drugs were stopped. In other words, our experience has been essentially the same as reported here.

Dr. T. Dewey Davis, Richmond: I have used Pregnenolone in a small series of arthritis of various types both parenterally and orally and have not seen a single patient derive any benefit from its use, nor have I seen any harmful effect.

As regards ACTH and Cortisone in rheumatoid arthritis, we have used these drugs in a number of long-standing cases with crippling deformity and intolerable pain. They have invariably shown improvement with disappearance or alleviation of the pain and their ability to use their extremities has been improved within the limitations of their permanent joint destruction. Our major problem has been the maintenance dose. Because of the expense we have attempted to keep it as low as possible; but in doing this we are very apt to give too small a dose. It is quite distressing to have one of these individuals relapse from their improvement and have their hopes dampened.

Up to the present time we have not seen any mental disturbances from either Cortisone or ACTH; but from reports in the literature I am quite sure that we will run into this problem in the near future. Fortunately, the complications of these drugs usually disappear fairly completely when they are withdrawn.

Dr. William H. Higgins, Sr., Richmond: Although the beneficial effects of Cortone are confined largely to the early or moderately advanced cases of rheumatoid arthritis, occasionally we do see miraculous results from this hormone in the totally disabled individuals. I would like to report a notable improvement in a man of sixty who was a victim of a deforming arthritis for forty years. He had marked ankylosis of his hands, feet and knees and it was with considerable difficulty that he could walk across his room with the aid of crutches. Naturally he could not shave himself and he was largely dependent on his family for assistance.

By the fourth day of treatment he was walking without crutches and without assistance and there was unfolded to him a new world. He can now feed and shave himself and although his movements are slow and awkward he now has a different outlook on life.

Witnessing this amazing change in an arthritic of long standing it is one of the greatest miracles within my knowledge.

Cortone is not a cure but it does bring relief to many unfortunate victims in a manner never believed possible.

New Books.

We give below some of the newer books received at the Tompkins-McCaw Library of the Medical College of Virginia, Richmond, which may be had under usual library rules by writing the Library:

Allen—The kidney, medical and surgical diseases.
A.M.A.—Handbook of nutrition. A symposium. 2nd ed.
Bowes and Church—Food values and portions commonly used. 7th ed.
Bray—Clinical laboratory methods. 4th ed.
DeSanctis and Varga—Handbook of pediatric medical emergencies.
Fleming—Penicillin. 2nd ed.
Hypertension, a symposium.
Kagan, ed.—Studies in pediatrics and medical history.
Lever—Histopathology of the skin.
Martin and Johnson—Practical microscopy. 2nd ed.
McEwen—Bacteriological technique.
Menkine—Newer concepts of inflammation.
Mommaerts—Muscles.
Perry—Scientific Russian.
Pickles—Haemolytic disease of the newborn.
Proceedings of the 2nd clinical ACTH conference. Vol. II. Therapeutics. 1951.
Proudfitt and Robinson—Nutrition in diet therapy. 10th ed.
Reese—Tumors of the eye.
Riese—Principles of neurology in the light of history and their present use.
Reynolds—Physiology of the uterus. 2nd ed.
Symposium on steroids in experimental and clinical practice.

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UROLOGICAL PROBLEMS IN INFANTS AND CHILDREN*

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C. W. BEAVEN, M.D.,
and
A. A. CREECY, M.D.,
Newport News, Virginia.

We would like to discuss for you today urological problems found in infants and children. Pathology of the urinary tract in young children, if thought of and properly investigated, will explain a lot of symptoms presented for proper diagnosis. Both congenital and acquired types are found. In presenting this subject it was decided to classify the conditions frequently encountered as follows:

1. Pathology in the urinary tract which accounts for masses in the abdomen.
2. Pathology in the urinary tract which accounts for recurrent attacks of abdominal pain.
3. Pathology in the urinary tract which can explain a fever of long duration.
4. Pathology in the urinary tract which can explain repeated attacks of pyuria with high fever, commonly known as pyelitis.

An investigation of the urinary tract in infants and children should include an adequate history especially pertaining to the urinary tract. It should include a complete physical examination, complete blood count and urinalysis, a tuberculin test, blood chemistries such as urea or NPN and creatinine as well as a urine culture, an intravenous pyelogram, also a cystoscopic examination and a retrograde pyelogram. Of these procedures examination of the urine, urine cultures and pyelogram are most important. Pus in the urine is a good indication of urinary pathology, but absence of pus in the urine does not always rule this out. The type of organism found in the urine is always of significance. For instance, if the urine culture shows the presence of the streptococcus or staphylococcus organism, the infection of the urinary tract is most likely secondary to infections elsewhere in the body, such as tonsillitis, boils, etc. If the urine culture shows a gram negative organism, most likely it would be the colon bacillus and the basic pathology would be found in the urinary tract and this pathology may be an obstructive or congenital lesion. If the history presents symptoms referable to the urinary tract and the colon bacillus is found in the urine, an intravenous pyelogram is indicated. It is best first to do intravenous pyelograms in infants and children because it is a more simple procedure. This procedure can be done in the office. It is not necessary to give an anesthetic and, of course, not necessary to admit the patient to a hospital. As a rule the intravenous pyelogram will give adequate information as to the type of pathology in the urinary tract. At times it will give suggestive findings and these findings should be further investigated with a cystoscopic examination and retrograde pyelogram. If the intravenous pyelogram is negative, most likely there is no pathology in the urinary tract. In doing intravenous pyelograms in infants and children, a large amount of diodrast is given intravenously, a larger amount than recommended by the manufacturer of this product. A test for sensitivity should be done before injection of the dye. The patients, except infants, are instructed to go without liquids and food for at least twelve hours before the procedure and the mother is instructed to give an enema early on the morning the patient is investigated.

The following cases will demonstrate conditions representing the four groups previously mentioned:

The first one is that of a mass in the left abdomen. This patient was a two weeks old male. The mass was about the size of an orange. Urinalyses were repeatedly negative. Urine cultures were negative. A barium enema revealed a normal large bowel. An intravenous pyelogram was not of great help, but showed some dye in the region of the left kidney. The kidney was not well outlined. Cystoscopic examination and retrograde pyelogram were not successful. An exploratory operation was done and a multilocular cyst of the left kidney was removed. The right kidney appeared normal. Since the removal of the kidney the baby has done well.

*Read before the Seaboard Medical Association, at Fort Monroe, Va., December, 1949.

From Hogg-Beaven Pediatric Clinic and Buxton Hospital, Newport News, Va.

In the second case, that of a newborn baby girl, the mass was first felt when the patient was about five days old. The mass was in the left abdomen. Urinalysis and urine cultures were negative. A barium enema ruled out any lesions of the large bowel. An intravenous pyelogram was not successful since the kidneys were not visualized due to a large amount of gas in the small and large bowel. A retrograde pyelogram was not successful due to an obstruction in the left ureter which prevented the injection of skiodan into the left kidney pelvis. A few days after this procedure an exploratory operation was done and a miltilocular cyst of the left kidney was removed. The progress of this child has been satisfactory since then. Intravenous pyelograms in newborns do not give us the proper information because of the large amount of gas present in the small and large bowel and also because of rapid excretion of the dye by the kidneys.

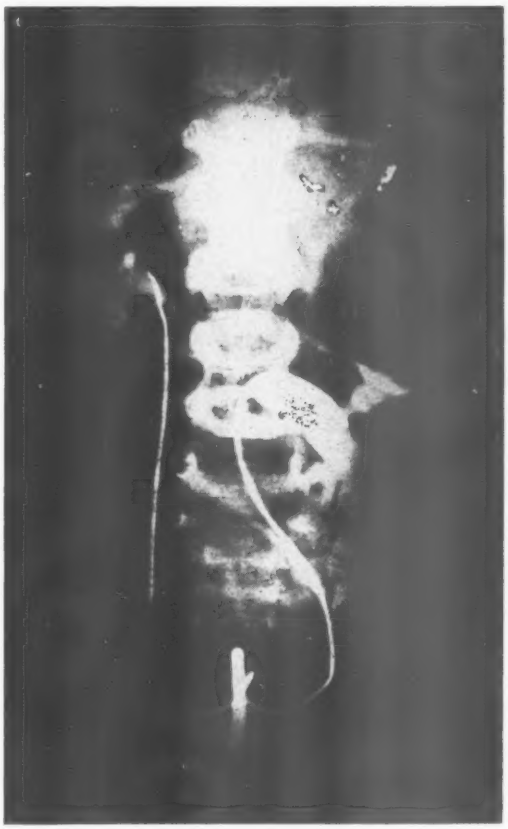

Fig. 1. Retrograde pyelogram.

The third case in this group is a boy twenty-two months old. When first seen he presented a mass in the left abdomen. Other than that he appeared well. Urinalysis was negative. Our impression before further study was that he had a Wilms tumor. A retrograde pyelogram was done and, as shown here (Fig 1), the radiograph revealed an abnormally placed kidney with large distorted left kidney pelvis. This mass was removed and later identified as a Wilms tumor. The boy is now thirteen years old. About eleven years have elapsed since the removal of his kidney. This is a rare instance in which a Wilms tumor has been removed and the patient has lived over five to seven years after removal. Each year we have taken x-rays of his chest and as far as we can determine there has been no metastasis. We believe that the chances for this boy's life are good. Ladd and Gross of Boston who have reported a large series of Wilms tumors advocate early removal of the tumor without preoperative irradiation, but they do advocate irradiation after the mass has been removed.

The following three cases will illustrate the second group, that is, recurrent abdominal pain:

The first case is that of a boy nine years old who presented recurrent attacks of vague abdominal pain. He was referred to us for study after the removal of his appendix which did not relieve his symptoms. When seen the general examination was negative. A urinalysis was negative and a blood count was normal except for an increase in eosinophiles to 12%. The examination of stool for ova and parasites was negative. A urine culture was negative. During early infancy this child had eczema. It was thought that his symptoms could be due to gastro-intestinal allergy. It was approached as such without results. Next, an intravenous pyelogram was done and this is what was found (Fig. 2): A hydronephrosis of the left kidney pelvis with definite constriction of the ureter about three centimeters from the pelvis. A retrograde pyelogram showed the same condition. He was cystoscoped with dilation of the ureter and a few weeks after the cystoscopic the pain subsided and he has been well since.

The second case is that of a boy thirteen years old who had been having recurrent abdominal pain for five years. A general examination was negative. A blood count was negative. A urinalysis was negative except for an occasional small clump of pus.

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Fig. 2. Intravenous pyelogram.

The urine culture was negative. An intravenous pyelogram (Fig. 3) revealed a large tortuous left ureter at the junction with the bladder. A cystoscopic examination and a retrograde pyelogram revealed caliectasis and pyelectasis of the left kidney and a stricture of the left ureter at the junction of the ureter with the bladder. Dilation of this stricture was done with some relief to the patient.

The third case in this group is that of a boy six years of age who complained of vague pain in the left side of his abdomen. This patient was observed over a period of a year. Our studies such as complete blood counts, urinalysis, examination of his stool for ova and parasites were negative. He was markedly constipated, having very hard dry stools. The pains in his left abdomen became worse. On one occasion he was definitely tender over his left kidney. An intravenous pyelogram was done which showed hydronephrosis of the left kidney. He was further studied with a retrograde pyelogram which showed a left hydronephrosis with obstruction at the uretero-pelvic junction. The hydronephrosis was thought to be congenital in type and the obstruction due to an aberrant vessel. On operation no aberrant vessels were present but a congenital fibrous band was found in the upper left ureter. This band was released and the opening enlarged. Six months after operation another retrograde pyelogram was

Fig. 3. Intravenous pyelogram.

done and the left kidney pelvis appeared to be much smaller and the constriction of the upper ureter had been lessened. The patient has not complained of any more abdominal pain since the operation.

The following case will illustrate a condition in the urinary tract which explains a fever of long duration. This patient is a ten year old girl who was seen by us about six months ago and who presented a history of having unexplained fever for the past two years. The fever would occur every one to two

months and last for a few days. Before seeing her she had had a complete study including an allergic investigation but not a culture of her urine because urine specimens did not show the presence of pus. When we studied her our investigation was negative except for the presence of a gram negative bacillus in her urine. The urine did not show pus at anytime. A urine culture was repeated and the same organism was found. It was classified as a colon bacillus. With this in mind a study of the urinary tract was done and an intravenous pyelogram (Fig. 4) showed suggestive clubbing of the calyces of the right kidney and also suggestive enlargement of the right kidney pelvis. A cystoscopic examination and retrograde pyelogram revealed subacute infection of the trigone of the bladder, a right calicectasis and a right hydronephrosis. This patient was given chloromycetin followed by a course of mandelic acid. After that therapy was given she did not have return of her spells of fever.

Fig. 4. Intravenous pyelogram.

This patient illustrates the fourth type, that is, repeated spells of pyuria with high fever. The patient was five years old when first seen. She gave a history of having repeated spells of pyuria with high fever since the age of three years. The urine was loaded with pus and a urine culture showed the presence of a gram negative bacillus which was classified as the colon bacillus. Otherwise this child was normal. Her tonsils were removed several months previously with the hope of preventing the recurrent attacks of pyelitis. With this history of repeated pyuria and the presence of a colon bacillus in her urine, an intravenous pyelogram (Fig. 5) was done and as you can see there is a constant filling defect of the right kidney. This patient was cystoscoped and a retrograde pyelogram was done. During the cystoscopic examination a stricture of the

Fig. 5 Intravenous pyelogram.

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right ureter was found at the junction of the ureter with the bladder. This was dilated and the patient was put on a course of mandelic acid and since that time she has not had a recurrence of the pyelitis. The constant filling defect in the right kidney proved to be a congenital bifid kidney. This, of course, had nothing to do with her pyelitis.

The cases just presented are patients of ours seen and studied in our practice in the past several years and I believe that they demonstrate fairly well the type of pathology which we may expect to find in infants and children. The type of therapy in dealing with this problem should, of course, be decided upon after the exact diagnosis is made. If obstructive lesions are responsible for the diseased urinary tract, then the obstruction should be relieved when possible. If infection is present, and most likely it is, such drugs as mandelic acid, sulamyd, streptomycin, aureomycin and chloromycetin should be used.

This paper was presented as a diagnostic pediatric paper. I have not brought anything new to you. The main purpose of it all is to emphasize that infants and children as well as adults present problems of the urinary tract and, if thought of and properly investigated, we can prevent real urinary tract damage and sometime prevent the loss of a kidney.

Reilef From Hemorrhoids, Episiorrhaphy Wounds and Cracked Nipples in the Parturient.

Postpartum distress from hemorrhoids, episiorrhaphy wounds, and fissured nipples is a common condition with many new mothers. Relief from these ailments, due to a lack of any competent specific agent has been primarily on an empirical basis, and has varied from simple nursing remedies to the use of opiates.

An ideal therapeutic measure, which is simple to use, effective in result, low in toxicity, and without hazard to patients is reported by Herbert E. Schmitz, Charles J. Smith, and George A. Carberry of Lewis Memorial Maternity Hospital, Chicago, main article in the March 1951 Western Journal of Surgery, Obstetrics and Gynecology. This agent consists of a topical anesthetic ointment containing 20 per cent dissolved benzocaine and oxyquinoline benzoate in a bland, water-soluble base.

76 patients with painful episiorrhaphy wounds were relieved in an average of seven minutes, with an average duration of 5.5 hours, duration of therapy 3.5 days. 11 patients suffering from fissured nipples were relieved in an average of 20 minutes. Duration of relief after one application averaged 5 hours, and duration of therapy 2.3 days. 13 patients with tender hemorrhoids were relieved in an average time of 10 minutes. Average duration of relief after one application was 6 hours, and average duration of therapy 4.4 days.

The authors conclude that the 20 per cent dissolved benzocaine ointment is a simple and effective means of relieving these common distressing discomforts in the parturient.

SPINAL FUSION IN THE TREATMENT OF LOW BACK PAIN—SOME CLINICAL OBSERVATIONS.*

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We have done 156 spinal fusions in the last 4½ years in our private practice, and of this group we have follow-ups on 137. The others were either discarded on account of poor records, or because the follow-up was less than four to six months. We have also followed with the other members of the Staff at the Veterans' Administrative Hospital, 55 cases. These cases at the V.A. Hospital are used for comparison because extra bone was used in these fusions. In my opinion the V.A. cases were even more carefully selected than our private cases because, here, we often have a compensatory element. These cases show about the same number of painful pseudo-arthrosis as our private cases did, and in this group we had three failures of fusions in spondylolisthesis, which is a little unusual. One of these cases could be traced to a local infection and one could not be accounted for.

In this paper no spinal fusion that was done for scoliosis, tuberculosis, etc., was reviewed for obvious reasons. The cases considered are those of mechanical weakness, due to congenital anomalies, such as sacralization of a transverse process, spina bifida, spondylolisthesis or old trauma. Localized arthritis and second disc explorations were other causes. We do not do a fusion at the first disc exploration unless there is a mechanical weakness also.

There are almost countless articles in recent years on spinal fusions of different types, each author claiming better results with his own modification of the two basic types, namely, the Hibbs and the Albee. In this paper we are dealing with one main factor, that is, the alleviation of pain and restoring the patient to a normal, or as near normal, life as possible. Some of these cases can get a perfect result clinically, yet by x-rays have a pseudo-arthrosis. Only by exploration can you be sure of a fusion[1]. Thompson and Ralsson reviewed one thousand and ninety-six spinal fusions done at The New York Orthopedic Dispensary and Hospital, and of this group they explored sixty-five cases which clinically and by x-ray examination led them to believe that they had a pseudo-arthrosis. They found fourteen of these solidly fused, showing 78.4 percent correct diagnosis under the best circumstances. We feel that the most important part in getting good results is in the choice of the patients. Most of my failures are due to this fact and not that the operation failed to fuse. With one known exception, the patients who were not satisfied or that I was not satisfied with, had very solid bony union, proven by multiple x-rays, after being followed for more than one year. This exception had complete absorption of all the bone chips and a second fusion was done, using iliac bone grafts. This patient, eventually, was much improved, but in this paper is counted as a failure.

In the selection of the patients, the evaluation of pain is essential. In this entire series all of these patients were operated on for pain and for pain only. The causes of pain in this series are listed below. The referring doctor can be of the greatest help in evaluating pain. Beware of the patient who has had many operations—this is as true here as it is in any surgery. Beware of the compensation case—these cases can be cured easily if the compensation is settled first. They can usually be cured if they have the right mental attitude and are having a great deal of pain. This pain, we prefer, should be present for a long time. We feel that the results in the Veterans Hospitals are good because (1) when a patient comes in with back pain, regardless of his x-ray findings (here again we are speaking of mechanical weak backs) he has conservative treatment and observation for a reasonable time. Much can be learned by the application of a cast and observation of a patient. A neurotic person tolerates it poorly with much gas and many complaints. (2) If a patient comes in with back pain and a desire for an increase in pension, he is treated much more conservatively. As above stated, all of these patients were operated on for pain. They had clinical and x-ray findings to back up this pain and responded to the treatment of the pain properly. All had con-

*Read before the Chesapeake and Ohio Surgeons' meeting, at White Sulphur Springs, West Virginia, November 14, 1950.

1. *Journal of Bone Joint Surgery*, April, 1949.

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servative treatment first, either by us or the referring doctor. Of course, many patients show the same x-ray findings that we call here mechanical weak backs and have no pain. That is why I try to stress the fact that we operated for pain in these cases and not because of x-ray findings or to obtain a spinal fusion. There were one hundred and fifty-six cases of which we analyzed one hundred and thirty-seven. The average age of these patients was 36.5 years. The oldest was 56, and this man had a ruptured intervertebral disc and a localized arthritis. The youngest was age 20, with a complete spondylolisthesis, and the 5th lumbar vertebra was sitting in front of the 3rd sacral segment. The duration of the symptoms averaged 4.3 years. The longest was 30 years. This was a spondylolisthesis. The shortest was one week, and this was a ruptured disc with a mechanically weak back. We found thirty-five cases to have discs throughout the 4½ years. There were only 10% with disc in 1946, in comparison with 30% in 1949. Thirty-three gave a history of trauma, or about 24%. We had six compensation cases which had not been previously settled. Of these, four went back to work with a 10% general disability. One had a 25% general disability; this man had a crushing fracture with some nerve involvement of three years' duration. One patient returned with no permanent disability so far as his accident was concerned. There were fourteen cases of spondylolisthesis, about 11%. Congenital anomalies, such as sacralized transverse processes, spina bifida of the 5th lumbar or 1st sacral segment with mechanical arthritis or previous disc operations, accounted for 57% of the operative procedures. We reviewed these cases by years, and it is interesting to note that we have done more fusions in each succeeding year. We hope and think that this is because our results are proving very satisfactory and not because our practice or our desire for surgery is increasing. We also note that we fused many more following disc surgery in 1949 and 1950 than previously. We feel that this is due to the unsatisfactory result after removing disc in mechanically weak backs. We have one patient who had a disc per year for three years. At the last surgery a fusion was done and we look for a fair result. We know that multiple operations about the spinal cord cause adhesions and residual pain, and require a longer recovery period. In studying our results for a period of eighteen months, we did routine flexion and extension x-ray examinations and found 6% failures of fusions. This is comparable to the results reported by other authors, but since so many of these were clinically well we gave up the practice of x-raying these patients in flexed and extended position. We felt that it was foolish to focus a patient's mind on his back, and if he thought that he was well, we certainly would agree with him.

The Operation—We feel that the type of fusion that should be done is the simplest to be satisfactory. Bosworth,[1] in discussing McBride's paper, stated that "future advances in the art of spinal fusions at the lumbosacral angle will probably not be due to surgical techniques but the future development of knowledge of the factors favoring bone growth and repair, both local and general, will undoubtedly help to reduce the percentage of pseudoarthrosis." In our group of patients, we used no extra bone except in a few cases in which there was a defect due either to previous laminectomy or to a large spina bifida. The group done at the Veterans Administration Hospital all had iliac or some bone from the bone bank. The results were about the same done by comparable surgeons. We use a modified Hibbs' fusion, being sure to turn up the layers of bones on the laminae and across the articular facets. This wide bed is essential. The bone obtained in this manner and the spinous processes are cut in small fragments, most of them grapenut in size, to be placed in the raw bed. Another important fact is to turn bone from the sacrum across the 5th interspace, greensticking the fragments, if possible. With a sharp angled gouge this isn't hard to do. This type of operation saves lots of time for the patient and our results are better than when we use extra bone. We feel that too much bone is detrimental, particularly cortical bone. Small fragments allow motions at many places and not much at any. Another advantage is that the patient does not complain of the donor site. Seldom is a transfusion necessary. We usually match the patient for transfusion, have the blood ready but seldom have to use it. The patients are put in a cast, half spica then or eight to ten days later. They wear a cast for six or eight weeks, depending on the patient and defect. They are started on back and abdominal exercises after four or five weeks and some are allowed up with cast on in five weeks. We do not use screws in

our spinal fusions. We feel, first, that they are unnecessary to obtain fixation, and, if used, we doubt if you would get fixation in soft bone for more than a few days at best. Of course, in boiled cadaver bone they give good fixation. Metal, even screws, often give pain in extremities; why not in a back? Should you get an infection, matters are worse. Roger Anderson may be right in his belief of no fixation, externally or internally, just leaving the muscle spasm to fix the graft in place. In special cases we have used none and they did well and fused nicely.

Post-Operative—We feel that early exercise plus no strain, no heavy lifting for six months is essential. Patients return to light work in ten to twelve weeks, laboring work six months. We feel that you should not use a brace post-operatively. This admits defeat and if the patient depends on the brace he will not develop the natural brace, namely muscles.

Our results were classified according to the patient's response to treatment, and, of course, cannot be too accurate: 1. The excellent results were the ones discomfort free within four months or less. 2. The good ones were the ones discomfort free in six to eight months. 3. The satisfactory ones were the ones still having some discomfort but who could return to their former occupation. Needless to say, this third classification depends, first, on the patient and, second, on the occupation. We have had them to return to almost all branches of work with the possible exception of coal mining. 4. The un-satisfactory ones were those who felt they were not improved by the operation. We had thirty-one excellent, or 22½%; forty-six good, or 34%; fifty-five satisfactory, or 41%; and five poor, or 3.5%. This gives us 95% or more satisfactory results. I would like to state again, regardless of how un-scientific this classification is, the purpose of the surgery was to relieve the patients of pain and, if they were satisfied, we feel that the result justified the means.

Conclusions

1. The choice of patient is most important.
2. The type of operation should be as simple as possible to obtain good results, and that extra bone is not essential and may be detrimental.
3. Internal fixation is not necessary and should not be used.
4. The time of recovery in some cases may be ten to twelve months or even longer.
5. Exercises started early are essential.
6. Spinal fusion in the treatment of low back pain is a good procedure.

Indiscriminate Use of Aspirin May Affect Blood.

Serious effects may result from the indiscriminate use of such salicylates as aspirin, according to a report in the September 8 J.A.M.A.

The case of a 74-year-old man who experienced eight years of continuous intestinal bleeding as the result of prolonged use of aspirin was reported by Drs. Walter Modell and Russel Patterson of the department of pharmacology and surgery, Cornell University Medical College, New York.

"Serious toxic reactions to the salicylates are rare in relation to the widespread use of this group of drugs," the report stated. "In the present case it was possible to establish a causal relationship between prolonged intestinal bleeding and the taking of acetylsalicylic acid [aspirin]."

The patient, according to the report, suffered from weakness, anemia and a decrease in the number of colorless blood corpuscles which are believed to aid in the clotting of the blood.

The symptoms disappeared with the discontinuance of the use of aspirin. However, the doctors pointed out, they were unable to determine positively the connection between the taking of the aspirin and the reduction of the number of colorless blood corpuscles.

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PULMONARY TUBERCULOSIS AND THE DOCTOR IN PRACTICE

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To accurately diagnose tuberculous pulmonary lesions in some instances today is more difficult than it has been in the past. This is chiefly because we are now fully aware of the innumerable conditions which can simulate pulmonary phthisis both clinically and roentgenographically. The tendency for the internist and chest specialist to proceed with some caution in labeling a pulmonary lesion tuberculous, unless there is some good evidence, preferably corroborative in nature, to substantiate such a diagnosis, is also a factor. The real question for discussion is just what constitutes such corroborative and substantial evidence in order to arrive at the conclusion that a given patient has active pulmonary tuberculosis, and what are the chances for the practicing physician finding such cases.

The hundreds of thousands of miniature screening X-rays being done today have given rise to more and more thought relative to this question in view of the diversified types of roentgen shadows and configurations disclosed in subjects, the majority of whom are asymptomatic and leading ordinary lives. Garland has enumerated eighty-nine (89) different conditions which, in his experience and otherwise, have been confused roentgenographically with pulmonary tuberculosis. This figure seems rather astounding and it is of course assumed that every condition he listed is *not* very *frequently* misdiagnosed as tuberculous. We do know, however, that a certain group of entities can be easily confused in this respect. It is not the purpose of this paper, though, to elucidate upon the differential diagnosis of pulmonary tuberculosis roentgenographically or otherwise. However, with the practicing physician receiving more and more reports derived from the follow-up roentgen studies of the lungs after micro-film screening as practiced today in the country, he will become increasingly concerned about the real signficance of some of these findings as reported to him, especially when further clinical investigation is a necessity in order to clarify the diagnosis. And, we should face the facts—without the practicing physician following such individuals, tuberculosis case finding is not properly organized. At the same time, the practicing physician himself can play one of the more important roles in initiating case finding, if not the most important in many respects. To quote Hilleboe, "Tuberculosis presents at once a challenge and an opportunity to the general practitioner. Thousands of persons who have tuberculosis go to private physicians for other illnesses and no official agency ever sees them—too often it is assumed that the control of tuberculosis is solely the health department's domain of action. This is not true, nor can it ever be true, so long as men practice the ancient art of medicine."

One may ask a few questions. What are the chances of a physician finding pulmonary tuberculosis today in an average practice? Is tuberculosis prevalent? If so, is it all active? Hasn't the death rate fallen appreciably over the years? Finally, how can I, a practicing physician, uncover such a disease which at times is so "silent"? In answer to the question concerning the falling death rate, the reply is "Yes." But this is not even a partial reassurance. Let us glance at the picture during the past few years and see what has happened to tuberculosis morbidity and mortality in the U.S. Between the period 1940 and 1947 the TB death rate declined from 45.8 to 33.5 per 100,000, per year, or 27%, while the registration rate of new cases rose from 76.4 to 93.3 per 100,000, an increase of 22%. Shown in a different way, during the period 1940-47, the actual number of deaths fell from 60,428 in 1940 to 48,064 in 1947, or 20%; but the number of new cases reported went up from 100,772 in 1940 to 133,837 in 1947, an increase of 33,065 or 33%. It then appears that death rate is a limited and inadequate index of the prevalence of the disease in the community. Case finding surveys, growth of the pop-

ulation, wartime strain, immigration of new susceptible groups have all probably contributed to a larger number of known tuberculosis cases. At the same time, extension of hospital facilities, abolition of the "means test" in certain areas, and widespread health education campaigns have resulted in a larger number of patients accepting hospitalization. It is probable that the trend toward more public health teaching in the curricula of our medical schools in the last few years have stimulated the more recent graduates to be more "tuberculosis conscious" than the older practitioners, which in turn, has contributed to case finding. Modern treatment of the disease, including rest, collapse therapy, surgery, antimicrobial therapy is increasingly reducing the mortality rate, though not necessarily preventing the outbreak of new cases. Approximately one-half of all cases of significant tuberculosis have no symptoms, or symptoms so slight as to escape notice. According to the National Tuberculosis Association estimate there are a quarter of a million unknown cases of tuberculosis in the U.S.—at least as many as there are known cases—and recent experience indicates that the unknown cases far out-number the known. In the 1948 mass survey in Washington, D. C. 4,098 cases out of 4,665 cases of tuberculosis discovered were previously unknown to the Health Department. Similar findings have been reported in all other large surveys.

In the greater Richmond area, an analysis of the results derived from the joint X-ray survey program put on in the last three years by the Richmond City Health Department and the Richmond Tuberculosis Association, co-ordinated with many other agencies, reveals that the over-all incidence of tuberculous lesions in a cross section of the population is a little better than one per cent. An average of .1 per cent of the cases found are active beyond question at the first examination. From .2 to .4 per cent require definitive follow-up study and careful watching. The remainder are regarded as inactive or healed. We now have evidence of the higher incidence of pulmonary tuberculosis in patients admitted to general hospitals as compared to the general public. Significant are figures from six general hospitals in this country which report incidences from 4.2 to 8.1 per cent reinfection tuberculosis determined by routine chest X-rays of all admissions, for variable periods. Then, why shouldn't the portals of our physicians' offices be a fruitful field for tuberculosis case finding? In the writer's opinion, it certainly is that. Now, how can the physician uncover the cases of pulmonary tuberculosis we know are prevalent in this day and time?

Ordinarily four basic steps are necessary for the diagnosis of pulmonary tuberculosis. They are:

1. Prove infection (tuberculin test).
2. Prove existence of a focus in the lung (history, physical examination, and X-ray).
3. Prove this focus to be tuberculous (examine sputum or gastric contents).
4. Prove that this focus is active (sputum examination, serial X-rays showing progression, reaction, etc.).

When one considers the history in a given case which is suspicious clinically or otherwise for pulmonary tuberculosis, inquiry is first made regarding the family history of this disease and then whether the case in question has been in contact with a known, and especially so-called, "open" case of tuberculosis. If there is positive information in these respects, how significant should we regard it? If such history is negative, how should it influence our thinking? In respect to a contact history, it can simply be stated that, as a group, contacts more frequently have tuberculosis than non contacts. It is now accepted that as far as the case finding is concerned, we may expect to find from 25% to 50% of all tuberculosis by merely examining the contact group alone. As a matter of interest, in a group of one hundred and thirty-six tuberculous patients surveyed at Pine Camp Hospital recently, including both white and colored patients, the over-all incidence of those with a family history of tuberculosis was 29.1% and those with a definite contact history 23.9%. Only those were put in the latter group who had a reasonable continuous contact with a known active case, usually beyond a month's period. The writer is convinced that while contacts are a group with relatively high incidence, this group should not *and cannot be given* exclusive attention. Expressed in other words, it appears that the modern trend of thinking should be towards the "endogenists" and their beliefs that we can explain the incidence in the non contact group by their "endogenous" theory, but, at the same time, we should be willing to accept "exogenous reinfection" as another principle in the pathenogenesis of this disease, especially on the contact group. While

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no serious writer over the years has ever challenged the causative role of the tubercle bacillus, the old equation, *human host plus tubercle bacilli = tuberculous disease,* is certainly not accurate as the discrepancy between the prevalence of tuberculous infection and that of tuberculous disease completely justifies this conclusion. The usual and scientifically wholly unjustified conclusion is that the greater frequency of tuberculosis is caused merely by exposure to infection. Since contact usually implies co-residence, a similar level of living conditions, particularly in regard to nutrition, and frequently varying degrees of consanguinity, infection is only one of the plausible factors which may explain increased tuberculous morbidity in the contact group. In brief, from the practitioner's viewpoint, when he is dealing with a contact or contacts of a known active case, it suffices to say he might "prick up his ears a little higher" and make sure this person is examined carefully, including X-rays, and followed by such serial examinations for a minimum of two years, and even longer when thought advisable. The lack of a contact history, however, should have no influence at all, in dealing with suspected tuberculosis in a given case.

In respect to family history, the impression for years has been that members of families with clinical tuberculosis are particularly apt to develop the disease and that the clinical course is similar in close relatives. The tendency has been dominant to explain the frequency of tuberculosis in family members by exposure to infection. Yet, the similarity of the clinical course in blood relatives cannot be so explained. The relative roles played by heredity and environment in the development of tuberculosis have been perennial subjects of discussion. Recently, experiments have shown that there is a considerable basis for the long held belief that heredity plays a role in the evolution of the disease even though that tuberculosis is not actually hereditary is an established fact. In short, in a given suspected case it might be said that a family history is a bit of evidence to be considered on the positive side. The more we consider this particular subject, the more we see a close relationship between infection from contact, environmental and hereditary factors, and, oftentimes, all three factors are directly involved.

The frequent absence of symptoms, or, at least, of symptoms alarming enough to send the patient to the physician, in many cases of pulmonary phthisis is well known in this day. However, these patients *are not all asymptomatic.* Any deviation from optimal health, existing for several weeks, must arouse suspicion unless satisfactorily explained by other definite findings. Many cases of pulmonary tuberculosis would be diagnosed months and, at times, years earlier than they are, if it were not so frequently assumed that fatigue, poor appetite, chronic anemia, vague gastro-intestinal disturbances, weight loss and a score of others, occur commonly without organic disease. It should be realized that such symptoms may be manifestations of active tuberculosis. Such diagnoses as "chronic bronchitis", as an example, so often hide in patients, tuberculosis, bronchiectasis, or bronchogenic carcinoma. The infinite variety of symptoms that pulmonary tuberculosis may cause confronts the physician with a challenge. There are no classic symptoms of pulmonary tuberculosis in this day. The former belief, as an example, that hemoptysis was a so-called cardinal symptom is now known to be in error. Some observers believe that bronchiectasis, as an example of one of the common causes of blood spitting, is leading the list in the relative incidence of this symptom.

It may seem trite but it is worth repeating here; the elicitation of physical signs is of value in the diagnosis of lung disease; the lack of signs does not indicate the absence of disease. Advanced pathologic changes may be present in both lungs without demonstrable physical signs. Disease of the bronchial elements is apt to be associated with an abundance of auscultatory signs; of the alveolar elements, with a paucity of signs. It is not the writer's idea to devaluate the need and application of physical examination of the chest towards the diagnosis of this disease, but to emphasize our limitation in this respect. At the other extreme the percussion finger and the stethoscope can play a valuable role in a sanatorium where the diagnosis is already established. Fellows compared the roentgen and physical signs in 280 patients with early pulmonary tuberculosis. Abnormal physical signs were present in only 21%. Sampson and Brown reported that, in 392 cases with advanced pulmonary tuberculosis with cavity on X-ray, in only 15% were there physical signs suggestive of cavitation. In spite of the lack of correlation between roentgenographic and physical findings, we must utilize physical examination of the

chest as one of our methods in the detection of this disease, and in many instances the existence of a pathologic focus in the lungs can be proven this way. The *absence of a tuberculous focus, however, can never be proved without an X-ray examination.* This is now a generally accepted fact. There is an apparent trend in the younger graduates, however, to almost completely disregard physical examination of the chest as being of any real value towards the diagnosis of lung lesions. This is definitely a wrong tendency for obvious reasons. There will be many times wherein physical examination is all we have in our armamentarium at a particular given moment, such as in the home, be it in the city or in an isolated rural area, or where, as an example, the patient is not in an ambulatory condition and we need all the information we can possibly obtain at the bedside in order to proceed with an optimum plan in the handling of that particular case. Some practitioners, again, seem to think a negative examination of the patient behind the fluoroscopic screen is "reasonable chest clearance." There is no greater fallacy. Even in expert hands the early parenchymal infiltrate can be easily missed by such an examination. It might be safely said that in a clinical evaluation of the lungs the fluoroscopic examination should always be supplemented by a roentgenogram. Finally, in this day and time, a complete and thorough physical evaluation and study is not complete without a chest roentgenogram.

Probably one of the most neglected of our older procedures is the simple tuberculin test. The technical details concerning this procedure will be omitted as this would entail lengthy discussion. We merely want to emphasize the value of this test which is generally not appreciated. Quoting Myers, "every person who reacts characteristically to tuberculin has tuberculous lesions, regardless of his state of health and the lack of other evidence. Such a person has tuberculosis just as certainly as the patient who is dying of the disease. The difference is just one of degree. In the person who is dying, the disease has evolved through various stages; but at one time that person could have been found to have no evidence of tuberculosis except the tuberculin reaction." Whether or not we agree fully with the statement is not important. We have to accept, that, *tuberculin makes it possible to distinguish between infected and non infected beings,* because only the former react to an intra cutaneous injection of tuberculin. Whether or not the reactor has clinical tuberculosis must be determined by other methods as the test does not permit differentiation between mere infection and disease. In clinical diagnosis the main function of the test is, in short, to rule out tuberculous disease. In general, the diagnostic value of the tuberculin test increases with the decreasing age of the patient. In children, particularly below the age of five years and especially below three years, a positive test means recent infection and, therefore, often active or potentially active disease. In addition, such a circumstance means an examination of all the adult contacts is required. In the great majority of instances the source case can be found. The popular patch test is especially valuable in the case of children where it may be advisable to avoid the use of needles. In addition, parents can sometimes be persuaded more easily to give consent to a tuberculin test if no injections, no needles, are employed. When dealing with a pulmonary lesion and tuberculosis is being considered in the differential diagnosis and without other corroborative evidence at hand, the tuberculin test should always be done and, if negative, may exclude tuberculosis. When it is positive, and when there is no clinching evidence at hand, it is merely another bit of information to add to the positive side of the evidence which will enter into our final analysis of a given case.

Unlike the positive tuberculin test, the finding of tubercule bacilli in the sputum is specific for the diagnosis of pulmonary tuberculosis. This is one function of the clinical laboratory of such outstanding importance that it overshadows the significance of all the other procedures combined. Towards a diagnosis of this disease the statement rests on these facts:

1. In a number of cases of pulmonary disease only the demonstration of tubercle bacilli can completely establish the diagnosis.
2. In the majority of cases of active pulmonary tuberculosis, the demonstration of tubercle bacilli is a quick and the only unequivocal method of diagnosis.
3. Finding tubercle bacilli in sputum (or by gastric lavage) proves the activity of the lesion present and indicates the need for treatment, unless and until proved otherwise.
4. Sputum examinations with negative results are

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frequently one of the most important criteria to exclude the diagnosis of pulmonary tuberculosis and to arrive at a correct diagnosis.

It has been emphasized again and again that all too frequently sputum examinations are not done with the proper care and technical perfection. The fault is not all in the laboratory. It starts with insufficient instruction for the patient by the clinician. Many patients need careful explanations as to what sputum is and as to the mechanism of expectoration —in the vernacular, if the patients background requires it. It is not intended here to discuss the technique of sputum examination. Yet, it must be pointed out how a sputum report should be evaluated by the clinician. For this, he should know whether it was really sputum that was examined and not saliva or nasal secretion. *Let us routinely have sputum examinations done routinely in our patients who are expectorating.* It has been estimated, incidently, that nearly four per cent of all persons who visit physicians offices are coughing or expectorating. The alert physician will insist upon a sputum examination of all such patients. The reward is sure to come, sooner or later. A final word concerning sputum examinations. Let's not stop at just one, two or three specimens in a given case. Not too infrequently it is that fourth, or sixth, or even twelfth specimen that proves to be positive.

CONCLUSIONS

1. The death rate of pulmonary and other forms of tuberculosis is not an accurate index as to its prevalence.
2. Examination of the so-called "contact group" alone as a case finding means would fall very short of our mark.
3. There are no classic symptoms of pulmonary tuberculosis in this day.
4. The absence of pulmonary tuberculosis can never be proved without an X-ray examination of the chest.
5. We should make use of the simple tuberculin test as an aid in the diagnosis of tuberculosis lesion.
6. We should strive to do more sputum examinations for the detection of acid-fast bacilli—particularly in our every day practice of medicine.
7. Pulmonary tuberculosis is still prevalent in spite of reduction in mortality rate during the past few years.
8. The general practitioner can and should play a major role in tuberculosis case finding.

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CLINICOPATHOLOGICAL REPORTS

From the Case Records of the Medical College of Virginia and the University of Virginia Hospitals

Harry Walker, M.D., *Editor*
William Kay, M.D., *Associate Editor*

Case No.: 71

A 53 year old, white, married housewife was first admitted to the Psychiatric Service for observation. She had persisted in pathological prevarications so much so that it was thought necessary for some psychiatric observations to be made. Physical examination was negative. The urinalysis and blood count were normal. The serum bromide level was 36 mgm.%, NPN 36 mgm.%, and blood sugar 100 mgm.%. Flocculation negative. ECG normal. Before adequate study was complete her release was requested and she was discharged with the diagnosis of psychopathic personality with schizoid tendencies.

Eight months later she was again admitted from an outside hospital because of fever of 104°F. Ten days prior to this her delusions again had become prominent, and she showed evidence of social deterioration. She had consumed a half-pint of whiskey, had fallen and struck her head against a radiator some five days before admission. The day of admission she had been placed in another hospital with high fever, which had subsided with intravenous glucose, penicillin, and aspirin. She had not eaten much in the last ten days. A urine specimen showed 2+ albumin, many red cells and a few white cells.

When first seen she was lying in bed, alert but restless. She appeared to be well developed, poorly nourished, and older than her stated age. Although acutely ill, she was responsive to questioning and was mildly euphoric. Anger was shown towards her husband, she was disoriented as to time, and insight and judgment was thought to be impaired.

Temperature 101.8°F. Pulse 120 per minute. Blood pressure 68/30. The head, eyes, ears, nose and throat were normal. The neck was negative and the chest clear. The heart sounds were regular, but rapid. The abdomen was soft and flat without masses or organs palpable. The extremities and neurological examination were normal.

Hemoglobin 14.6 grams; RBC 4,940,000, WBC 11,700 with 84 polys., 12 lymphs., and 2 monos. A catheterized urine specimen was straw, cloudy, and acid with specific gravity 1.018, 2+ albumin, 2+ sugar, and negative acetone. There were many granular casts, 1-2 WBC/HPF, and 16-18 RBC/HPF. NPN 43 mgm.%.

She was given 4 cc. of paraldehyde, but promptly vomited it. She was then given 10 cc. of adrenal cortical extract intravenously. The blood pressure was 84/40 and an hour and a one-half later was 104/60, and two hours later 98/40. An ECG showed sinus tachycardia and abnormal T waves; "it was quite abnormal since previous tracing eight months ago". She was also given streptomycin, penicillin parenterally, and terramycin orally. During the night 2000 cc. of intravenous fluids and 10 cc. of adrenal cortical extract were given. Hypotension persisted and she was apparently in or near shock levels for at least eighteen hours. She was given 1000 cc. of whole blood with rise in blood pressure to 105/60 but twelve hours later it had gradually declined to 70/50. During this day she was seen by a consultant who found shock a predominant feature. The abdomen was slightly distended and tympanitic without rigidity or spasm. Acute tenderness was present over both kidneys and output in twelve hours only 120 cc. against an intake of 1500 cc. Other laboratory work at this time showed: Urine—acid, cloudy, specific gravity 1.015, 2+ albumin, 1+ sugar, 30-40 RBC/HPF, occasional WBC/HPF. Blood: Hbg. 15.6 grams, RBC 5,210,000, WBC 27,250 with 95% polys., 3 lymphs., and 2 monos. A smear taken for malaria showed "leukocytosis, marked toxic granulation, and Sohle bodies. Platelets appear reduced. No malaria seen". Sodium 134, potassium 4.0, chlorides 102 meq/L respectively. Blood sugar 148 mgm.%. She was given adrenal cortical extract and caffeine.

In the next twelve hours the blood pressure had risen to 90/70, and twelve hours later to 120/90. Urinary output remained poor. Spinal fluid was normal. Agglutinations negative.

The next day CO_2 was 23 meq/L and NPN was 80 mgm.% with creatinine of 6.3 mgm.%. Chlorides 102 meq/L. Clinically the temperature was subsiding and she was more rational. Two days later

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the blood pressure had risen to 160/100 and ranged between 140-160 systolic over 90 to 100 diastolic for the next five days. She developed abdominal distention. Her mental status varied between clearness and confusion. She vomited frequently. The distention persisted but she was passing gas rectally. Temperature became normal.

A chest plate taken on admission suggested pneumonitis in the left lower lung field. A flat plate of the abdomen five days after admission showed the large bowel markedly distended. A chest plate disclosed some density in the right lower chest suggesting atelectasis. A barium enema was normal.

The sodium and potassium remained normal, spinal fluid was normal and culture negative. The urine was loaded with red cells and specific gravity was now 1.010 on several occasions. The NPN was 80 mgm.% with a creatinine of 7.5 mgm.%. Leukocytosis persisted and RBC was 5,720,000 with 18.1 grams of hemoglobin five days after admission. The NPN rose to 128 mgm.%, creatinine 9.0 mgm.%. A serum bilirubin was normal. Bleeding and clotting time normal, prothrombin concentration 50%. An ECG showed auricular tachycardia.

Ten days after admission the blood pressure began to fluctuate markedly, respiration became labored, and the abdomen again greatly distended. The urinary output now was 60-70 cc. every twenty-four hours, and the hematocrit rose to 61% with 22 grams of hemoglobin. She had been receiving prostigmine. She had continued to vomit and had become drowsy. A Wangensteen suction was instituted and she had several large liquid stools. In the last thirty-six hours temperature rose to 102°F., she was in shock and in spite of all treatment the blood pressure could not be elevated. She developed labored breathing, became cyanotic, and died on the thirteenth hospital day.

DISCUSSION BY DR. WILLIAM M. ANDERSON.*

This case is that of a 53 year old, white, woman, who was first seen in this hospital because of a psychiatric disorder, characterized by "pathological prevarications"—or in other words deviating from the truth to an abnormal extent. This symptom must have been very contrary to the patient's usual character, otherwise she would not have been hospitalized for it. All laboratory studies on this admission were within normal range except the blood bromide which was elevated (36 mgm.%), this level usually does not come with psychotic behavior. The patient left the hospital before any treatment could be given. The discharge diagnosis was psychopathic personality with schizoid tendencies.

We then lost sight of this patient for a period of eight months. It would be useful for our purpose to know whether her symptoms persisted, progressed, or abated during this period, but the protocol does not supply us with this information.

We next heard of the patient when she was readmitted to the Medical College Hospital following a ten day illness in which her delusions became more prominent and other evidence of social deterioration became apparent. She fell five days prior to admission and struck her head, but there is nothing else in the record which would make one think that this had any bearing on the final outcome. On the day of admission she had been seen at another hospital where high fever was noted to subside following treatment with glucose, penicillin and aspirin. Her urine was said to show two plus albumin and many red blood cells at that time.

On admission to the Medical College Hospital she was alert, but restless. She appeared euphoric, was disoriented as to time, exhibited anger toward her husband (which may or may not have been abnormal for her), and demonstrated poor insight and impaired judgment. She had fever of 101.8°F., pulse rate 126 per minute and a blood pressure of 68/30. Her physical examination was otherwise not revealing. The laboratory work was essentially normal except for a slight leukocytosis (11,700) with some shift to the myeloid series, two plus albuminuria, glycosuria, many granular casts and 16-18 red blood cells in the urinary sediment. The NPN was 43 mgm.%.

She was treated with ACE intravenously and the blood pressure rose temporarily. Treatment was also begun with Streptomycin, Terramycin, penicillin, I. V. fluids, whole blood and more ACE. In spite of this she was "in or near" shock for 18 hours. An electrocardiogram on the day of admission showed a rapid rate and what was described as "very abnormal T waves". This finding is rather non-specific and not of much help at this time.

On the second hospital day, the blood pressure was still low and a consultant was impressed with shock.

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The abdomen was distended and tympanitic, and the CVA were acutely tender bilaterally. This latter observation may prove to have been one of very great importance. During 12 hours of this second day the patient excreted only 120 cc's of urine in spite of an intake of 1500 cc's. The urine again showed two plus albumin and 30-40 red blood cells. The serum sodium was a little low (134 meq/L.) but potassium and chloride were normal. I think the glycosuria and blood sugar of 148 mgm.% have to be disregarded since this patient doubtless was receiving much I.V. glucose in an attempt to keep the blood pressure up. The white blood count by the second day had risen to 27,250 with even more shift to the left and the appearance of toxic granulation and Döhle bodies. I understand that this toxic granulation is a rather non-specific finding and is often seen in association with severe infections, as well as in some cases of carcinoma. The presence of so-called "hair cells" was not mentioned. It would be of some interest to know whether these were found, since they are regarded by some hematologists as indicative of neoplasm. Döhle bodies are cytoplasmic inclusions which were orginally found in the granulocytes of most patients with scarlet fever. Since this original discovery they have also been noted in other coccal infections and I am not aware of any other significance which might be attached to them.

At this time a lumbar puncture was done and the spinal fluid found to be normal. Agglutination tests were also negative. The patient was treated with more ACE and caffeine, and the blood pressure fluctuated at near normal levels. Her urinary output continued to be poor.

On the third hospital day her NPN had risen to 80 mgm.% and creatinine to 6.3 mgm.% (normal 1-2 mgm.%). This could have been the result of inadequate glomerular filtration resulting from the low arterial pressure. Her temperature was down and she appeared more rational.

No mention is made of the 4th hospital day, so we may assume that the patient remained about the same.

The patient's condition from the 5th to the 10th hospital day changed from time to time but no definite trend was noted. Her blood pressure stayed up around 160/100. Her mental status varied. She vomited often and abdominal distention was a problem. Gas was passed by rectum, however, and x-rays of the abdomen and chest were made.

The patient's temperature remained normal, serum sodium, serum potassium, and spinal fluid were all reported to be normal. The urine, however, was again loaded with red blood cells; the NPN went from 80 mgm.% to 128 mgm.%, creatinine from 7.5 mgm.% to 9 mgm.%; and the leukocytosis persisted. The red blood count and hemoglobin began to show evidence of severe hemoconcentration. Other laboratory data obtained during this period were: a normal bilirubin, a normal bleeding and clotting time and a prothombin concentration of 50%, which is not low enough to cause bleeding. The electrocardiogram again showed auricular tachycardia.

On the 10th hospital day (or 20th day of terminal phase of her illness) her blood pressure began to fluctuate more, respiration was labored, abdomen distended and she passed only 60-70 cc's of urine in 24 hours. Hemoconcentration became much more severe (hemoglobin 22 grams). She vomited frequently, appeared drowsy, and passed several large liquid stools. Her temperature was 102°F. This situation persisted in spite of treatment and the patient died in shock and cyanosis on the 13th hospital day—or 23rd day of terminal illness.

To summarize briefly—this patient was a 53 year old white woman who from the standpoint of history and symptomalogy had an illness of nine months or 23 days' duration, depending on whether one believes the early psychotic symptoms were part of the final illness or were entirely unrelated, and who, in addition to the psychiatric complaints, exhibited cyanosis, anorexia, vomiting, oliguria, and diarrhea terminally. From the standpoint of physical signs, she showed intermittent fever, a distended tympanitic abdomen, bilateral costo-unilateral angle tenderness, persistent hypotension and tachycardia, and finally death in shock and cyanosis.

Laboratory studies revealed two plus albuminuria, hematuria, leukocytosis with a shift to the left, toxic changes in the leukocytes, severe hemoconcentration, steadily rising non-protein-nitrogen and creatinine in the blood and a slightly lowered serum sodium.

The x-rays showed lung lesions and a distended colon.

The electrocardiogram revealed auricular tachycardia and abnormal T waves.

Her response to treatment with adrenal cortical

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extract was questionably good, while the effect of antibiotics was even more uncertain. Various supportive measures were at times helpful, but she died 23 days after the onset of her terminal illness.

In approaching the differential diagnosis in this case, I think that there are four main phases of the patient's illness which need discussing: (1) psychiatric, (2) circulatory abnormalities, (3) evidences of infection, (4) urinary changes.

There are four possibilities regarding the connection of this patient's psychiatric symptoms with her final illness: (1) They represented a primary personality disorder without organic basis and were entirely unrelated to the terminal disease. (2) The psychiatric disease might have caused another organic disease, as for example alcoholism might lead to cirrhosis of the liver, or a depressed person might take poison. Bichloride of mercury poisoning could have been responsible for some of the symptoms seen in this patient. This aspect will be discussed later. (3) The psychiatric symptoms might have represented a primary organic disease. The personality deterioration, abnormal mood, pathological lying, alcoholism, etc., are sometimes seen in a patient having a lesion in the frontal lobe. But against a primary neurological disease would be the normal spinal fluid and the absence of any other neurological signs. (4) The psychiatric disorder might have been part of a generalized disease or secondary to disease elsewhere in the body. Infection, however, would not be a suitable explanation here since there was no evidence of infection on the first admission when pschiatric symptoms were prominent. A neoplasm with distant metastases in the brain could not be ruled out, however, and might offer a suitable basis for this picture.

The second striking feature of this case was the persistent hypotension and finally death in shock. The oliguria and azotemia might be thought of as secondary to the hypotension but the possibility of a primary renal factor in their pathogenesis should be considered. Among the causes of shock, the simplest and most obvious is hemorrhage. Certainly this patient did not bleed externally and there was no evidence of bleeding into the gastro-intestinal tract. Furthermore the shock of hemorrhage is usually associated with hemodilution and lowered hemoglobin (after several hours), while the reverse was true in this case. Failure of the heart to pump blood into the periphery may cause shock, but when it occurs it is most often associated with myocardial infarction, and in this patient we have neither the typical chest pain nor the electrocardiographic findings of this condition. Shock in this patient was like the shock associated with severe burns where serum escapes from the intravascular space and blood volume is lowered. A similar condition may occur whenever extensive tissue damage occurs. Sometimes an overwhelming infection of one sort or another can produce this type of shock. And we do have in this case classic signs of infection—fever, leukocytosis, shift to the myeloid series, and certain granular changes in the cytoplasm of the leukocytes. It is difficult, however, to think of an infectious agent which alone would produce a course such as this. If infection were present, I believe that it played a secondary role to some other underlying disease.

In any case of unexplained persistent hypotension one should always think of adrenal cortical insufficiency. This may be of two clinical types—acute or chronic. The latter is known as Addison's disease and is characterized by bronzing of the skin, low blood pressure, weight loss, weakness, anorexia, low blood glucose, low serum Na and Cl and high serum K. The skin of this patient was not pigmented and the electrolytes were pretty normal, and I do not think she had Addison's disease. Acute adrenal cortical insufficiency in a person with previously normal adrenal glands, however, is not associated with bronze skin, and the electrolytic changes in the blood may not become apparent immediately. This syndrome is associated with nausea, diarrhea, vomiting, shock, costo-vertebral angle pain, weakness, hyperpyrexia, prostration, and death. To support this diagnosis we have the clinical picture, borderline low serum Na, the blood pressure response to adrenal cortical extract, and the absence of any other adequate explanation for shock. The usual etiology of acute adrenal cortical insufficiency is either hemorrhage into the adrenal glands with destruction of the parenchyma or thrombosis of the adrenal veins.

It seems unlikely that infection such as meningococcemia occurred here and caused destruction of the adrenals. There were no petechiae or other signs of bacteremia and the duration of the illness would not be in keeping with that diagnosis.

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The evidences for infection in this case were the intermittent fever with questionable response to antibiotics, severe leukocytosis with shift to the left, and toxic granulation in the cytoplasm of the leukocytes. Many of the patient's symptoms could have been the result of infection. If we assume then that infection was present, it is necessary to decide whether it was the primary disease or occurred secondarily to some other disease. In trying to make this decision it might be helpful if we ran through some various specific infectious agents in hopes of finding one which is known to produce a clinical picture similar to this patient's. Certainly, I can think of no filtrable virus which would cause a disease of this duration with leukocytosis. Rickettsial diseases are usually associated with a skin rash, which this patient did not have. Among the bacteria no coccal or bacillary infections would be likely to produce this picture without some evidence of bacteremia or of localization of an inflammatory process. Fungal infections or parasitic infestations do not fit the picture. Among the spirochaetes, however, there is one disease which at least superficially resembles that which this patient had; namely, Weil's disease. This is characterized by fever, leukocytosis of marked degree, vomiting, slow pulse (early in the disease), petechial hemorrhages and aching in the muscles. The onset is rather sudden and "grippe like", and about the fifth day jaundice becomes noticeable and oliguria sets in. (30% of the cases are said not to show jaundice.) When death occurs it takes place usually between the 9th and 16th days. This patient, however, probably did not have Weil's disease for the following reasons: There was no history of suitable exposure; jaundice would be expected in a patient who died of the infection; there was no response to penicillin; and usually the spinal fluid in Weil's disease shows an elevated cell count and xanthochromia, which this patient did not have. Thus none of the infectious agents seems to fit the picture very well. We are then left with the possibility that if infection was present it was probably secondary to some other underlying disease.

The fourth striking set of abnormalities in this case were those of the urine: namely, two plus albumin, many red blood cells, and many granular casts; and of these the hematuria seems most important. The possibility of this having been the result of catheter trauma is unlikely since it was present in many examinations. It would be impractical to consider all of the possible causes of hematuria. Some of the more likely ones, however, might be ruled out as follows: Nephritis would be associated with hypertension and red blood cell casts in the urine, neither of which was present here. Hematuria due to urinary calculus is likely to be painful and would not be expected to cause death in shock. Renal tuberculosis is characterized by hematuria, but tuberculosis is usually recognized elsewhere in the body and the urine also contains inflammatory cells. Other bacterial infections may cause urinary bleeding but are invariably associated with pyuria. Infarction of the renal parenchyma is manifested by hematuria, and kidney pain, but this circumstance is usually the result of emboli which lodge in renal arteries and arterioles, having come most often from endocardial vegetations or thrombi. This case presented no evidence of endocarditis. Blood dyscrasias may be associated with hematuria. In this case the bleeding and clotting time were normal and the prothrombin time 50% which is not low enough to cause bleeding. No mention is made in the protocol of the platelets or of the clot retraction time. The description of the smear did not suggest leukemia. A condition known as "lower nephron nephrosis" is characterized clinically by oliguria, shock, vomiting, hemoconcentration, blood in the urine, albuminuria, granular casts in the urine and a rising NPN. The blood pressure often is seen to fall to shock levels on the first day of illness, to then rise to about normal levels on the second day, and afterwards to hover in moderately hypertensive levels. Edema may or may not be present. This patient's clinical picture certainly seems to fit this syndrome. The question is whether the lower nephron nephrosis was secondary to shock from some other casue or whether the shock was due to the lower nephron nephrosis which was in turn due to some unknown cause. Other known causes for the lower nephron syndrome are transfusion reactions, severe trauma to muscle, extensive burns, and reactions to sulfa drugs. Carbon tetrachloride when inhaled will damage the lower nephron and produce a picture like this, and it is not necessarily associated with obvious liver disease. Persons who are chronic alcoholics or have recently ingested alcohol are known to be hyper-susceptible to the effects of carbon tetrachloride. Possibly this patient with her personality

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deterioration became alcoholic and somehow or other was exposed to this chemical. I do not believe that this can be ruled out. Bichloride of mercury ingested with suicidal intent will produce renal damage with oliguria, etc., but here we usually see abdominal pain, blood streaked vomitus, loose bloody stools, collapse, delirium, convulsions, and death often within the first 2 or 3 days of illness. There are two other rather rare conditions which should only be mentioned: necrotizing papillitis of the kidneys which may be fatal and which occurs in diabetics. I do not think this need be considered further. The other condition is known as bilateral cortical necrosis of the kidney. This usually occurs in toxemia of pregnancy, but occasionally is seen during infectious diseases. The pathological picture is that of thromboses and hemorrhages throughout the kidney, and the clinical characteristics are anuria or oliguria with hematuria and elevated NPN. The etiology is unknown but is thought to be related to certain vasomotor changes in the kidney. I see nothing in this case to support this diagnosis. In unexplained hematuria one should always think of neoplasm somewhere along the urinary tract. I do not believe we can rule out that possibility here. The presence of a mass in the region of the kidney or a filling defect in an I.V. pyelogram would have firmly supported such a diagnosis but we have the benefit of neither in this patient. The hematuria then remains unexplained but, of all the possibilities mentioned, neoplasm and lower nephron nephrosis would seem to be the ones least ruled out.

If we suppose that this patient really did have a carcinoma of the kidney, the most likely type would be the so-called hypernephroma or Grawitz tumor. This is a relatively slow growing tumor in adults which may be asymptomatic for many months and sometimes is first announced by symptoms from a metastasis. The frontal lobe lesion in this case might then be such a metastasis. This tumor then characteristically invades the renal pelvis, causing hematuria, and later extends into the renal vein. The adrenal vein on the left usually empties into the renal vein and thus would be occluded. This tumor has been known to grow out into the vena cava and up as high as the right auricle of the heart. It would not require too much imagination then to see how such a circumstance might also involve the right adrenal vein which empties into the vena cava directly. Thus, with both adrenal veins occluded, the occurrence of adrenal cortical insufficiency would be inevitable. Pulmonary and hepatic metatases might also be present since they are known to occur. Bronchopneumonia alone or in combination with necrosis of tumor tissue might explain the fever and leukocytosis. This explanation is certainly far from established and is presented merely as an interesting possibility.

I think that the important diagnostic clues in this case were hematuria in a fatal illness in which kidney tenderness, oliguria, and shock were features. This to me would tend to localize the primary disease to the kidney. The evidences of infection, the hypotension and shock, the hemoconcentration may all have been secondary. The question as to what the basic renal lesion was remained unanswered, but if I had to take my pick I would say lower nephron nephrosis due to some unknown toxic substance such as carbon tetrachloride which she inhaled soon after ingesting alcohol.

HOSPITAL DIAGNOSIS: Adrenal cortex insufficiency, cause (?).

DR. ANDERSON'S DIAGNOSES: 1. Adrenal cortical insufficiency. 2. Lower nephron nephrosis (? etiology).

PATHOLOGICAL REPORT: Dr. Gordon R. Hennigar*.

The heart was of normal size and weight. The myocardium was pale, soft and flabby—an appearance not infrequently seen in anemia, shock and severe infections.

Except for bilateral basal atelectasis, the lungs were not remarkable. The liver, pancreas and gall bladder showed no special pathological change. In none of the organs, either at autopsy or gross conference, could any focus of active infection be discovered.

The right and left kidneys weighed 170 and 180 grams, respectively. The cut surface revealed accentuation of the cortical vascular markings and congestion of the pyramids. Both adrenal glands were the "seat" of hemorrhagic infarctions. The latter were situated primarily in the medullae of the glands. The right weighed 18 grams and the left 13 grams. The right gland was more extensively involved than the left (fig. 1). Thromboses in the adrenal veins

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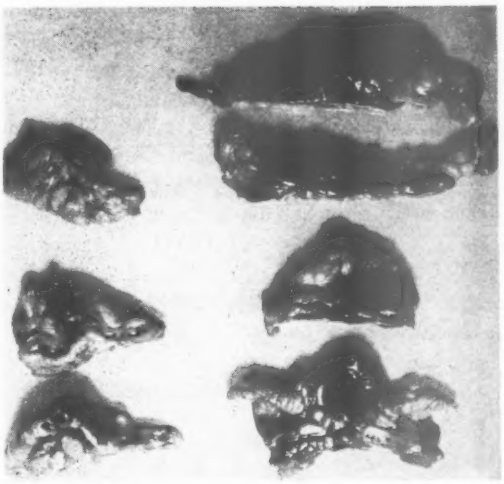

Fig. 1—Cross sections of the adrenal glands. The larger one reveals extensive hemorrhage.

were noted grossly as well as microscopically (fig. 2).

This case was selected for discussion today not only because of its challenging clinical aspects, which Dr. Anderson executed in a most admirable fashion, but because it presented some features which from the standpoint of pathogenesis of lower nephron nephrosis and adrenal hemorrhage are obscure even to the oldest of morphological investigators.

First of all, let us deal with the lower nephron nephrosis. We attribute the kidney lesion, in this case, to the secondary shock resulting from the rapidly developing hemorrhagic infarctions of the adrenals. The common causes of lower nephron nephrosis are: incompatible blood transfusions (hemoglobinuric nephrosis), burns, mercury poisoning, severe acute hemorrhage, eclampsis, septicaemia, crush syndrome, heat stroke, and intoxication by the sulphonamide group of drugs. Except for the latter, scrutiny of this list shows that the common denominator is secondary shock. To reiterate, the pathogensis of so-called lower nephron nephrosis is far from clear. Time and time again, patients die in a state of shock and oliguria from one or more of the various causes listed above and when the kidneys are examined at autopsy we fail to find the gross and microscopic features of classic lower nephron nephrosis. Furthermore, another discrepancy arises. As in this case presented today, the kidneys grossly will reveal nothing other than congestion and yet microscopically present the features of lower nephron nephrosis. Seldom do we grossly see the injected region next to the medulla described by Trueta[1] and referred to as the juxta-medullary shunt.

Fig. 2—Section of the left adrenal to illustrate an hemorrhagic infarction involving the medulla and adjacent zona fasciculata. Note the thrombus lying in an adrenal vein in the center of the field.

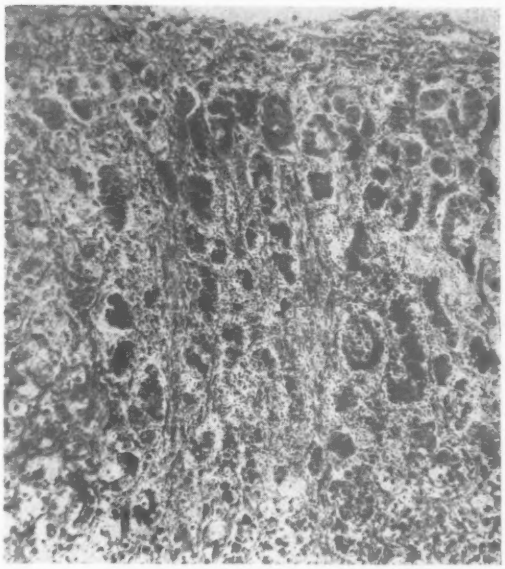

Fig. 3—Adrenal. The zona glomerulosa is indistinct. Loss of polarity of the adrenal cords of the fasicular layer. Patchy necrosis is present.

The term lower nephron nephrosis is without a doubt a misnomer. True, the lower nephron, which comprises the ascending loop of Henle and distal convoluted tubule suffer the "brunt" of the attack, the proximal convoluted tubule may show necrosis.

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Grossly, the kidney of lower nephrosis is larger than normal, pale with a thickened, bloodless outer region of the cortex. The juxtamedullary portion of the cortex and pyramids are injected and cyanotic. Microscopically, one sees casts of hemoglobin or heme in the distal tubules and collecting tubules, cloudy swelling, fatty infiltration and necrosis of tubular epithelium, regeneration of tubular epithelium, lymphocytes and edema in the interstitial tissue.

It is our belief that the disturbance in renal function in lower nephron nephrosis is dependent on changes in the afferent and efferent arterioles to the nephron unit. The change is one of calibre of the vessels such as occurs in shock.

Our reason for this is based on a clinical observation. Namely, patients will in shock develop oliguria or anuria for 10-20 hours, then suddenly, without therapy, undergo spontaneous diuresis or normal urinary output. It hardly seems feasible that this mechanism is dependent on regeneration of tubular epithelium. The heme casts seen in the tubules are not abundant enough to cause generalized intrarenal obstruction. The heme casts *per se* have not been shown to induce necrosis of the adjacent tubular epithelium. Lastly, the red cells and protein in the tubules come from the blood in the glomerular capillaries. The mechanism here would be one of vasoconstriction of the afferent arteriole with glomerular hypoxia resulting in increased capillary permeability of the glomerular filter.

Having shed no light on the pathogenesis of lower nephron nephrosis, let us now turn to that of the bilateral adrenal vein thromboses with hemorrhagic infarctions of these glands. Here, again, we feel far from adept to explain the cause of this phenomenon which was the probable cause of the death of the patient.

Blood cultures and blood smears from the heart were negative. In view of the antibiotic therapy, however, this is not surprising. There was no evidence grossly or microscopically of pneumonia, or genitourinary infection. Whenever we are confronted at autopsy with adrenal hemorrhage, septicaemia is our first thought as the etiology. Almost every known bacterium has at sometime or another been incriminated as playing a role. I am sure, however, that we are very capable of missing a focus of infection at autopsy. Certainly, as Dr. Anderson has pointed out, the fever, leucocytosis with shift to the left of the differential Schilling Count, toxic granulation, Döhle bodies, all were highly suggestive of infection.

The second cause of adrenal hemorrhage is adrenal vein thrombosis, which is frequently bilateral. We have often questioned whether or not a large percentage of these cases might not be thromboses, secondary to an underlying infection. It is feasible to believe, I think, that in severe septicaemia we may expect foci of necroses in the adrenal cortex from which venule thrombosis might occur and then extend to involve the larger adrenal veins. The frequently listed causes of adrenal hemorrhage are given in table 1. It is interesting that Wyatt[2] recently reported a case of bilateral adrenal vein thrombosis with infarctions, accompanied by lower nephron nephrosis. No etiology was determined. This was the first case of lower nephron nephrosis associated with adrenal hemorrhage reported in the English literature. Recently, we had a 72 year old patient who fell and sustained bilateral fractures of the wrists and fracture of the arm. One week later she went into shock and died. Autopsy disclosed bilateral adrenal hemorrhage with adrenal vein thromboses. The patient had been on penicillin therapy prophylactically so that autopsy cultures were meaningless. Microscopically, the adrenals in the case today showed indistinctness of the zona glomerulosa. The reticulum framework of the cortex was destroyed. Patchy necrosis was seen here and there. Most of the nuclei of the zona fasciculata were pyknotic and the cells of the zona reticularis were atrophy with loss of lipoid.

TABLE 1

PATHOGENESIS AND ETIOLOGY OF ADRENAL HEMORRHAGE

1. Septicaemia—meningococcus, staphylococcus, influenza virus, etc.
2. Thrombosis with infarction due to circulatory stasis, e.g., cardiac failure, shock.
3. Hemorrhagic diatheses.
4. Burns.
5. Idiopathic.

Table 1—Etioloy of adrenal hemorrhage.

The remainder of the anatomical findings comprised the following: petechial hemorrhages in viscera and brain, vacuolation eosinophils of pituitary, bilateral hydrothorax, healed chronic pyelonephritis, dilatation of pancreatic acini, basophilic (mucopolysaccharide) change of aortic media.

The proposed pathogenesis in this case is shown in table 2.

TABLE 2

PATHOGENESIS

? INFECTION ⟶ PROGRESSIVE, BILATERAL ADRENAL VEIN THROMBOSIS WITH MULTIPLE INFARCTIONS.

↓

SHOCK ---- ANOXIA, PETECHIAL HEMORRHAGES, FOCAL NECROSIS LIVER, GENERALIZED EDEMA.

—— LOWER NEPHRON NEPHROSIS

↓

DEATH

Table 2—Proposed pathogenesis.

Pathological diagnoses:

1. Bilateral adrenal vein thrombosis with infarctions.
2. Lower nephron nephrosis (hemoglobinuric nephrosis).
3. Convolutional atrophy brain.
4. Bilateral basal atelectasis lungs.
5. Acute splenic tumor (acute splenitis).
6. Granulocytic hyperplasis bone marrow.

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PUBLIC HEALTH

Laboratory, Virginia State Department of Health

Intrastate Serodiagnostic Evaluation Study, January 1952

Premarital legislation in Virginia enacted in 1940 requires, as a prerequisite to the issuance of a marriage license, a serologic test for syphilis to be made at a laboratory approved for that purpose by the State Health Commissioner. Additional legislation was enacted in 1950 requiring prenatal tests for syphilis to be made in approved laboratories. Approval is based largely on demonstrated efficiency of test performance. The State Health Department, in accordance with provision of the above legislation, is planning to conduct an evaluation study of serodiagnostic tests for syphilis, to begin about January 15, 1952. All private, semi-private, and public health laboratories within the state which wish to be approved for the performance of premarital and prenatal serodiagnostic tests for syphilis have the privilege of participating in this study.

These studies are conducted in the same manner as the National Evaluation Studies and the standards of proficiency are those set up by the National Committee on Evaluation of Serodiagnostic Tests for syphilis. A brief description of the methods used in previous studies follows.

Specimens of whole blood, half of them from syphiltic and half from non-syphilitic donors, were collected and distributed to the participating laboratories at the rate of ten a day for four days a week until approximately two hundred specimens had been distributed. Each laboratory upon receipt of the blood performed its test (or tests) and sent the results to the central laboratory of the State Health Department for tabulation of sensitivity and specificity ratings.

Blood donors were selected and their clinical status determined by syphilologists of the Medical College of Virginia Venereal Clinic. All blood was collected at the clinic and was distributed to the participating laboratories by the State Department of Health. The Venereal Disease Laboratory of the U.S. Public Health Service and the Central Laboratory of

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the State Department of Health acted as control laboratories.

Sensitivity ratings were compiled by giving one credit for each positive result obtained on a syphilitic donor, one-half credit for doubtful and no credit for negative results. Specificity ratings were obtained by giving one full demerit for each positive result and one-half demerit for each doubtful result on a presumably non-syphilitic patient.

These ratings were based on the clinical status of the donors rather than the serological results obtained by the control laboratories. The National Committee on Evaluation of Serodiagnostic Tests for Syphilis considers satisfactory test performance to be a specificity rating of not less than 99 percent and a sensitivity rating within 10 percent of that of the control laboratory.

The purpose of these studies is threefold; one, to evaluate test performance of the laboratories within the State in order to have a sound basis upon which to approve them for performance of premarital and prenatal tests for syphilis; two, to stimulate an interest in better serology; and, three, to aid the laboratories in improving the quality of their test performance.

The necessity for improvement of the quality of test performance is obvious when one considers that in the first intrastate evaluation study (April, 1940) only nine of thirty participating laboratories (30%) achieved the national standards on one or more tests. The results of the last study (May, 1950) in which seventy-eight laboratories participated and sixty-three (81%) achieved saitsfactory results, shows that a very marked improvement has been made. The fact that a standard is offered whereby the laboratory may check its test performance is valuable in itself because it is impossible to know whether one is performing serologic tests satisfactorily unless one has an opportunity from time to time to check that performance with a standard.

It has been our observation that failure to achieve satisfactory ratings is usually due to one or more of the following causes: inadequate equipment, reagents of poor quality, antigen which is not sufficiently sensitive, or to lack of training of the serologist.

The State Health Department wishes to do everything within its power to aid laboratories in improving the quality of test performance. Technicians from the various laboratories are welcome to visit the State Health Department Laboratory in Richmond. Here they consult the chief serologist about their problems, learn the latest technics and become familiar with various kinds of new equipment. If they wish they may perform serologic tests under the supervision of the serologist, and in this way correct their own defects and improve their technic. They may stay as long as they wish.

In the past, this has been of great benefit to the laboratories. For example, in the study of 1948-1949 several laboratories failed to attain ratings high enough to qualify for approval. Most of these serologists came into the Central Laboratory and worked with the serologist until they had solved their problems. In the next study (1950) the ratings attained by these laboratories were exceptionally good.

A serologist from the Central Laboratory will be sent to inspect equipment and to make suggestions for its improvement if a request for this service is made.

Since it may not be generally known that the State Health Department offers these services, and since their benefit is of much greater value to a laboratory before the study is undertaken than after it has failed to achieve satisfactory rating, arrangements may be made now for visiting the State Laboratories by addressing a request to:

Director of Laboratories, Box 1877, Richmond 15, Virginia.

Distribution of blood specimens will begin in January, 1952. Visits to the laboratory should be made sufficiently long in advance to enable one to obtain any new equipment, reagents, etc., in ample time to have them in working order before the examination of check specimens begins.

MONTHLY MORBIDITY REPORT OF THE BUREAU OF COMMUNICABLE DISEASE CONTROL

	Aug. 1951	Aug. 1950	Jan.-Aug. 1951	Jan.-Aug. 1950
Brucellosis	12	4	54	39
Diarrhea and Dysentery	423	532	1,765	2,708
Diphtheria	4	5	76	102
Measles	163	84	13,681	2,476
Meningitis (Epidemic)	0	6	82	91
Poliomyelitis	55	312	96	550
Rocky Mountain spotted fever	17	21	52	58
Scarlet fever	14	32	702	589
Tularemia	6	4	30	25
Typhoid and paratyphoid	6	16	36	57

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Medical Society of Virginia Cancer Committee

Chairman, GEORGE COOPER, JR., M. D.

Medical School Building, University, Virginia

Reprints of this and preceding Bulletins may be obtained from this office

October 1, 1951

Case Reports

Case I. A 64 year old man was referred to a Tumor Clinic for a palliative colostomy to relieve distress due to progressively severe obstruction of the sigmoid by an inoperable carcinoma with pelvic metastases. The referring doctor stated that he had first seen the patient eighteen months before, at which time he gave a history of bouts of low abdominal cramps, constipation and bloody diarrhea, weakness, and fever. Symptoms had been present for about a year, were becoming more frequent. Rectal and proctoscopic examinations were negative, but x-ray examination demonstrated "diverticula of the sigmoid, and a deformity probably representing carcinoma." A surgical exploration was performed. Extensive infiltration and fixation of the sigmoid was found and there were numerous enlarged glands in the areas of regional drainage. The surgeon felt that there was no need of a biopsy to establish the obvious diagnosis of carcinoma of the sigmoid. Also he felt that the palpable lymphatic metastases were too extensive to attempt a surgical cure so he simply closed the wound, later advising the patient and his physician that a colostomy should be performed when obstruction became more severe. As obstructive symptoms were now quite severe and the patient's general condition was deteriorating, the physician sent him to the Tumor Clinic to have his colostomy. Again, rectal and proctoscopic examinations were not helpful. The x-ray findings were reported as demonstrating an extensive sigmoid diverticulitis and a deformity, not characteristic of carcinoma, but so severe that the possibility could not be ruled out. At exploration, the sigmoid was found incorporated in a bulky hard mass and numerous enlarged glands were found. On frozen section of several of the glands and of several biopsies from the mass, the pathologist reported he could find no carcinoma, only inflammation. Therefore surgery was confined to resection of the involved length of bowel and an end-to-end anastomosis. Careful pathological study of the surgical specimen revealed no carcinoma, only an unusually severe chronic inflammation, apparently due to diverticulitis. The patient made a good recovery and resumed activities in which he had not been able to engage for several years.

Case II. A 53 year old woman was hospitalized for study because of symptoms suggesting a partial obstruction in the left side of the colon. The outstanding finding of a complete study was the x-ray demonstration of sigmoid diverticulosis and a pronounced deformity of the sigmoid interpreted as representing inflammatory changes secondary to diverticulitis. The patient responded nicely to antibiotics and was discharged after a second x-ray study by means of barium enema had demonstrated a partial disappearance of the sigmoid deformity. During the next six months, recurrent symptoms led to repeated x-ray studies and additional treatment on three occasions. Varying degrees of diverticulitis were reported by the roentgenologist until the last examination when a change in the contour of the deformity was noted, suggesting the development of a carcinoma in the area of diverticulitis. At surgical exploration, a bulky mass was found in the upper sigmoid and also many enlarged glands. Frozen sections were reported by the pathologist as showing carcinoma in both the biopsy from the mass and in one of several glands. Nevertheless, a length of bowel including the mass was resected and an end-to-end anastomosis performed. The patient did nicely for nearly a year, then with the appearance of liver and abdominal masses, a downhill course began which, in spite of palliative radiation therapy, ended in death two years after operation.

Comment: 1. Case I is another example of what can happen when biopsies are omitted because of reliance upon inspection, palpation, and clinical judgment. A patient who never had cancer at all was diagnosed as having a hopelessly advanced cancer. He endured eighteen months of mental anguish and physical incapacity when all that time he was suffering, not from incurable cancer, but from a chronic inflammation amenable to surgery.

2. In Case II, the stage of the cancer when exploration was finally resorted to makes it almost certain that the lesion had been present when earlier x-ray studies were done.

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The tumor had simply been obscured by the diverticulitis. Too great reliance upon roentgenological interpretation led to a fatal delay in correct treatment. Roentgenological interpretation is no more a substitute for pathological diagnosis than is clinical judgment.

3. Though there is no evidence that diverticulitis predisposes to carcinoma, these conditions are both fairly common in the sigmoid and may co-exist. The two cases demonstrate the confusion that readily arises. The demonstration by x-ray examination of a sigmoid diverticulitis should serve to alert all physicians involved to the possibility of concomitant carcinoma. If the diverticulitis is severe enough to alter the bowel contour significantly, surgery is usually indicated, both to find out whether an obscured carcinoma is present and to resect the diverticulum bearing portion of the bowel.

4. In Case I, even if his clinical diagnosis had been correct, the first surgeon showed poor judgment in not resecting the sigmoid. When the primary tumor is resectable, it should be removed, even though distant metastases are demonstrable, to relieve obstruction and to remove a source of hemorrhage and infection.

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MENTAL HEALTH

Joseph E. Barrett, M.D.,
Commissioner, Department of Mental Hygiene and Hospitals

Recreational Therapy at Lynchburg State Colony

At our Lynchburg State Colony every effort is made to use all forms of therapy recognized as standard procedure in the treatment of our patients. During the past five summers we have included in the recreational therapy program at the Colony organized camping parties under the supervision and guidance of the Chaplain's Department. In planning this program it was considered that, although this was to be a recognized therapeutic procedure, it might be carried out without too much regimentation and administrative handling which would be a deterrent to its effectiveness. The following is a resumé of this activity and the results accomplished as reported by Mrs. Raymond Morgan, Chaplain at the Lynchburg State Colony.

The first summer's project was accompanied with caution and anxiety. The camp staff was confident that the program should be free and spontaneous, but how would patients react when accustomed restraints were removed? Maybe some would run away. Because of this and other possible problems the first camping group was restricted to female patients who were carefully screened to eliminate behavior problems and possible elopers. Included in the group were epileptic and mentally defective patients, ranging in age from 17 to 30 years.

The camp was to be a vacation for some who would otherwise have no such opportunity. Believing that one of the principles of life is sacredness of personality, we directed our efforts continuously toward enhancing the dignity of each member of the group. To facilitate this feeling and to promote a sense of "togetherness" staff and patients worked and played together, ate at the same tables and slept in the same dormitories. Inequality of abilities was taken for granted but it was assumed that each had a contribution to make which was needed and wanted by the group.

Freedom prevailed; a minimum of regulations was recognized. Rules grew out of group discussion, and were self-imposed. All were led to understand that they were necessary in order for the group to live happily and comfortably together. The camp schedule was informal and flexible. It included organized and unorganized games, hikes, picnics, swimming, simple handicrafts, dramatizations, story hours, much singing and opportunity to just sit and observe the sights, sounds and smells of the woods. Swimming for the most part meant having fun in the outdoor pool, although some learned to swim and a few to dive. Neither work nor play was compulsory; instead, an effort was directed toward creating an atmosphere in which all would want to share in all activities.

Morale was high at all times. Not one untoward incident occurred. During the week only two girls out of the thirty were taken aside for individual counseling.

It was truly a week full of new experiences. Only one person had been in camp before; few had been in swimming. Sitting, talking, singing and listening to stories around a camp fire was a first experience for most of the group. To be utterly trusted was a rare experience for many. Some of the enjoyments of the week were expressed by the girls this way: It is so good not to have doors locked—to be able to go in and out of doors as you please." "I like to be where folks try to be friendly." "The freedom is wonderful." "It is fun to work at camp." "I like best the camp fires at night—being out of doors when it is dark." "I like the way we go on hikes; we don't have to walk two by two."

The first summer's experiences convinced the camp staff that when patients believed that they are being trusted they have great capacity to carry through. On the basis of this judgment the campers for the next two summers were selected only for physical fitness and included men, women, boys and girls. Several behavior problems were included to see how they would respond to the freer camp environment. In one instance a group of 40 boys, aged seven to eighteen who never go out of doors unattended at the hospital, made up a camping group. It was found that this group required very little more effort

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to supervise than any so-called normal group of boys.

During the summer of 1950 a group of forty older women, 40 to 67 years of age, made up a camp unit. None had ever been camping before. Many had not been away from the Colony in years; some not since they had been admitted. Three of these women asked on their second day at camp to be returned to the Colony. The environment was too unfamiliar; they were lonesome. But the others enjoyed it. Even the oldest went on hikes twice a day, splashed in the pool, or watched others doing so; spent hours at handicraft, enjoyed camp fires, and took great pride in keeping the camp clean. Their enjoyment was expressed in such statements as: "Don't this fireplace remind you of home?" etc. Said one to a staff member, "I never dreamed I would ever be sitting next to you eating a meal". Said another, "Do you suppose we could visit that little country church again? It is such a pretty church. You know, that was the first time I have sat in a real church in 13 years!"

At the end of last summer the Lynchburg State Colony Camp closed its fifth annual season. Four hundred and forty patients participated. There were four one-week periods of regular camping, accomodating forty patients each—two weeks for male patients and two weeks for female patients. There were seven one-day picnics; forty patients attended each time.

Camp is no longer a therapeutic experiment at Lynchburg State Colony. It is now one of its accepted efforts toward meeting the needs of its patients.

MEDICAL SOCIETY OF VIRGINIA

Public Relations

In dealing with the perpetual problem of physician-patient relationship, a recent article, reprinted by the American Medical Association, from *American Magazine*, recounts some age-old sources of patients' complaints. Not only does the author reveal these maladies in public relations, but goes on to recognize that a degree of satisfaction has been enjoyed by many of the disgruntled.

Referring to the survey made by Dr. John T. T. Hundley of Lynchburg, the article adopted his fundamentals of patient discontent which were declared to be in part: "money-grabbing doctors"; "overspecialization", widening the cleft between doctor and patient; use of technical terminology in answer to patient's questions; unwillingness by some to make home calls; excessive waiting for appointments. With the core of complaint thus established, the source of satisfaction was sought.

The grievance committee supplied at least a major portion of the answer. By what method could a grievance committee atone for the alleged misdoings of its medical colleagues? With the harm already done, it could only serve as a medium for redress. The dissatisfied could tell their story to an impartial and understanding group. Assuming the grievance justifiable, what avenues of action were advisable as well as effective?

A study of grievance committee files revealed several categories of action taken in response to various complaints. Four general paths of action evolved. Conciliation adjusted some ninety per cent of the largest lament, fees. Warnings by their professional peers sufficed in a number of instances. The strongest sanction would seem to be expulsion from the medical society or a recommendation that the physician's license be revoked. In difficult cases of improper treatment, reparative measures were taken; perhaps a specialist would be called in to advise. Applying these rules of remedy, grievance committees have espoused numerous otherwise strained and unyielding breaches of the doctor-patient bond.

The setup of a grievance committee might follow a general pattern inviting complaints of all kinds from the public. Of course, both patients' and physicians' version of the story should be heard along with a review of other evidence. Many situations will resolve to a simple misunderstanding easily cured when discussed openly.

Pursuant to an established policy, cases in which a malpractice suit has been started will not be con-

sidered by a grievance committee until a decision has been rendered. Seeking to avoid such suits with the attendant, bad publicity, and financial loss, many medical societies urge their members "to report promptly any medical error which may be a potential source of complaint."

Again, unlike a number of references to patients' complaints, the study uncovers that something constructive is being done. It is well to note that the house-cleaning efforts of the medical profession are producing results—results which will in time enhance the important physician-patient relationship.

Reprints of the article referred to above will be sent to the chairmen of grievance committees of compoent medical societies. Copies are also available for members upon request to the Medical Society office.

WOMAN'S AUXILIARY TO THE MEDICAL SOCIETY OF VIRGINIA

President—MRS. C. M. McCOY, Norfolk
President-Elect—MRS. HERMAN W. FARBER, Petersburg
Recording Sec'y—MRS. L. BENJAMIN SHEPPARD, Richmond
Corresponding Sec'y—MRS. LEMUEL MAYO, Portsmouth
Treasurer—MRS. KALFORD W. HOWARD, Portsmouth

The President's Pin

At the annual meeting of the Woman's Auxiliary to the Medical Society of Virginia in Roanoke in 1947 the late Mrs. E. Latane Flanagan of Richmond made a recommendation, which was accepted by the assembly, that a pin be purchased to be worn by the President of the Woman's Auxiliary to the Medical Society of Virginia during her term of office.

Mrs. Flanagan made a motion that a committee be appointed to consider a design and costs of a pin. Carried. The committee was as follows:

Mrs. P. M. Chichester, Chairman
Mrs. H. A. Latane
Mrs. J. E. Hamner
with Mrs. J. L. DeCormis, Ex-officio.

There was a ruling that the emblem used on the pin worn by the President of the Woman's Auxiliary to the American Medical Association could be used only in connection with National Auxiliary matters.

Many designs were considered and costs submitted. A report was given at the Board meeting on March 1, 1949. Mrs. Reynolds asked for further discussion at the annual meeting.

At the pre-convention meeting in October, 1949, Mrs. Holderby made a motion that the committee be authorized to make the final decision about the design and price of the pin and order the same. Carried.

Mrs. H. W. Rogers made a motion that the main motion be amended to provide for a larger committee to share in this responsibility. Carried.

Mrs. E. Latane Flanagan and Mrs. R. M. Reynolds were added to the committee, and Mrs. Holderby, Ex-officio.

The committee asked for suggestions.

Mrs. Edward Ray spoke of the staff of Aesculapius with its encircling snake which has been adopted as an insignia by the American Medical Association.

As an Auxiliary, we are permitted to use only half of the insignia of the American Medical Association.

The recommendations of the Board concerning the pin were accepted at the annual meeting 1949.

The design accepted by the committee was the triangle of Peyton M. Chichester, Jr., son of Dr. and Mrs. P. M. Chichester of Richmond. Its use was authorized by the President of the Woman's Auxiliary, American Medical Association.

The pin is of platinum. It is an open triangle with the upper half of the Staff of Aesculapius and the encircling snake placed diagonally across, with a medicinal leaf added. There is a three point diamond in each angle. On the upright sides of the triangle are Woman's Aux. — Med. Soc. Va. and across the base the word President. The pin was made by Schwarzschild Bros., Inc., Richmond. It has been worn by Mrs. C. E. Holderby, who presided at the 1950 meeting, and is now worn by Mrs. C. M. McCoy, the present incumbent.

A small pin of the same design can be purchased by the Past-Presidents. The die will remain the property of the Auxiliary.

The chairman of the committee feels that the

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triangle is significant of the cooperation of the patient with the physician and God in the art of healing.

Committee
MARIE C. CHICHESTER, *Chairman*
(MRS. P. M. CHICHESTER)

Other members of the Committee are:

MRS. H. A. LATANE *MRS. E. LATANE FLANAGAN
MRS. J. E. HAMNER MRS. R. M. REYNOLDS
MRS. J. L. DECORMIS, MRS. C. E. HOLDERBY,
Ex-Officio *Ex-Officio*

*Deceased 1950.

Northampton-Accomac Auxiliary.

On July the 10th, a number of members of the Auxiliary enjoyed a delightful outing on the cruiser "Rambler" out of Wishart's Point Yacht Harbor to Assateague Island Coast Guard Station as the guests of Mrs. C. E. Critcher. At the meeting held at this time, the Auxiliary voted to furnish draperies for the Grace Wilkins Holland Memorial Room in the Northampton-Accomac Hospital.

The slate for 1952 officers of the Auxiliary was presented by Mrs. Edmund Henderson, chairman of the Nominating Committee, and was accepted as follows: President, Mrs. John Wise Kellam; vice-president, Mrs. W. L. Cosby; secretary, Mrs. W. Carey Henderson; and treasurer, Mrs. John Rogers Mapp.

CATHERINE R. TROWER,
Chairman Press and Publicity

BOOK ANNOUNCEMENTS

Philosophy for the Common Man. By HEINRICH F. WOLF, M.D., New York. Philosophical Library, New York. 1951. xxxii-189 pages. Price $3.50.

Written by a doctor of medicine for the general reader who is interested in philosophical problems, and not for the professional philosopher, this book approaches these problems from the standpoint of modern science based primarily on the As-If philosophy of Hans Vaihinger. The author feels that the study of metaphysics is not only useless but harmful for the general reader. He therefore touches on aspects of ancient philosophy, continues with a mechanistic explanation of animal and human functions, and then concludes with discussions on free will, the purpose of life, and religion and the philosophy of As-If among other subjects. Dr. Wolf's approach is certainly an interesting one and should prove valuable to those who, like himself, are seeking a more serene outlook on life.

M. A.

Clinical Laboratory Methods. By W. E. BRAY, B.A., M.D., Professor of Clinical Pathology, University of Virginia; Director of Clinical Laboratories, University of Virginia Hospital. Fourth Edition. St. Louis, The C. V. Mosby Company. 1951. 614 pages. With 119 text illustrations and 18 color plates. Price $7.25.

The mere fact that Dr. Bray's Manual of Clinical Laboratory Methods has its fourth edition and was reprinted many times, speaks for itself. The book is used by a large group of people interested in the field of Clinical Pathology. Also worth mentioning is the fact that the book grows and expands with the field which it covers.

The Fourth Edition has 579 pages with many color plates and drawings, 43 new methods and modifications are included in the text, and newer antibiotics are discussed. An excellent cross-index helps to recommend this book as a great aid in troublesome situations which may arise in the performance of routine tests. A list of normal values can be found at the end of the book.

However, we have yet to see a book written to suit all persons interested in the field. We would like to see in the next edition, a chapter explaining the principles of spectrophometry. Blood Chemistry could be enlarged to equal in volume Bacteriology and Hematology.

In general, this book should be recommended for laboratories in small hospitals and doctors' offices for whom it seems to be designed.

H. G. K.

Handbook of Nutrition. A Symposium Prepared under the Auspices of the Council on Foods and Nutrition of the American Medical Association. Second Edition. New York, The Blakiston Company. 1951. xviii-717 pages. Price $4.50.

This is not a handbook in the usual sense of a guidebook or a manual of compiled data. It is a

comprehensive symposium on the present status of nutrition in its broadest sense. Much new information bearing on man's nutritive problems has accumulated since the First Edition of 1943. The Handbook consists of recent papers by leading authorities in all phases of nutrition. They are reprinted from *The Journal of the American Medical Association* with some additions and were prepared under the auspices of the Council on Foods and Nutrition of the American Medical Association.

In reprinting the series in one volume the American Medical Association has done an admirable job and produced a handy and valuable reference work. The 700 pages are divided into four main parts—The Individual Nutrients (including much on their roles in metabolism), Nutritional Needs, Nutritional Deficiencies (including a chapter on Fluid Therapy) and Foods and their Nutritional Qualities. The book is of convenient desk size and will be a ready and authoritative reference to current nutritional knowledge and problems.

L. D. A.

Pioneer Doctor. LEWIS J. MOORMAN, M.D., with and introduction by HENRY A. CHRISTIAN. University of Oklahoma Press. 1951. 252 pp. illustrated. Price $3.75.

From Cousin Henry's delightful introduction to the author's well told pilgrimage to the home of Francis Adams in Banchory, this attractive little book is filled with facts and stories of medical interest, and who is not interested in medicine today. There are stories of frontier life, obstetrical stories, sanatorium stories and Indian stories. The stories are all good, but the frontier stories suffer perhaps from the author's neo-classical diction. This reviewer has the feeling that a Will Rogers or even a "Dizzy" Dean could have told them better.

I was interested to note that my former fellow townsman, Dr. James N. Ellis, founded the American Medical Association of Vienna in the last decade of the 19th century. Dr. Moorman found the headquarters of this Association, with its registration system, its library and sub-post office helpful when he went to Vienna in 1909 for graduate study.

There is a good historical account of the sanatorium treatment of tuberculosis and an excellent chapter on medical education. His description of the patient-physician relationship, which he says must never be lost, can not be improved upon. "It is as fundamental as the family, as sacred as the church, as essential as free speech, and as right as anything in the Decalogue."

M.P.R.

Handbook of Pediatric Medical Emergencies. By ADOLPH G. DeSANCTIS, M. D., Professor of Pediatrics and Chairman of the Department of Pediatrics, Post-Graduate Medical School, New York University-Bellevue Medical Center; Director of Pediatrics, University Hospital, and Gouverneur Hospital, New York City. And CHARLES VARGA, M.D., Instructor in Pediatrics, Post-Graduate Medical School, New York University-Bellevue Medical Center; Assistant Attending Pediatrician, University Hospital and Gouverneur Hospital, New York City. St. Louis, The C. V. Mosby Company. 1951. 284 pages. With 51 Illustrations. Cloth. Price $5.00.

This book as the title indicates is a handbook giving in more or less outline form the therapeutic approach to conditions encountered in pediatric practice which call for rapid, emergency treatment. It does not attempt to be by any means a complete text of pediatrics, but should serve as a source of quick reference to obtain vital information in situations where there is no time for wading through comprehensive textbooks or locating a specific journal one vaguely remembers reading. The material gathered over a period of years, is presented in concise form and contains specific valuable detailed information, such as drug dosage for all age groups.

This book gives a comprehensive list of poisons, their principle clinical effects with antidotes or treatments. Also, a list of common household and commercial sources of poisons is given with their active ingredients. This may at times be invaluable to both doctor and patient when confronted with the ingestion of a product with unknown active poisonous ingredients.

A description of common pediatric diagnostic and therapeutic procedures accompanied by pictures and diagrams occupies one section. This book answers many questions concerned with medical pediatric emergencies which a doctor asks himself in a frustrating acute situation, where the proper course of action alone may be lifesaving. All in all, this to me is a wonderful systematized collection of vital information necessary to the modern practice of pediatrics, and I recommend it as a member of the reference library of the intern, pediatric house officer, pediatrician and general practitioner.

R. F. T.

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EDITORIALS

The Doctor's Wife

IF THE physician is the flower of civilization (such as it is) as Robert Louis Stevenson says he is, what shall we say of the physician's wife?

In preparing the series of editorials on "Doctors for whom the public should be thankful" we were impressed by the important role that the wife played in the careers of many of these doctors. One, and by many he was considered the wisest of the thirty-two, did not marry. He lived to be eighty-four. As he approached his 80th birthday he went to Boston to deliver an address on "Medical libraries and their aims" and Cushing had to clean a number of spots off his waistcoat. This is the only published evidence that "Popsy" Welch ever needed a wife.

One married after he had become famous. His wife was more interested in dancing and society than she was in making a home for him. In a few years they separated and finally were divorced. Later he married a home loving girl and was very happy. Koch was the only one of the thirty-two who behaved like the popular notion of a genius. His first wife bore him a daughter and died several years later. His second wife was devoted to him and gave him a microscope. When he divorced her he received a cold shoulder in Berlin and his former friends in Clausthal demolished the tablet they had placed on his boyhood home. He brought his third wife to the United States in 1910 for the International Congress in Washington and Trudeau amusingly said of the marriage: "You could not blame Koch, but what on earth could this young woman see in him?"

Mettauer and Brown-Sequard also married three times, but these six marriages were all terminated by death. The remaining 27 medical geniuses married only once, but the married state lasted through a long life. For the most part they were happy marriages. Mme. Bernard was jealous of her husband's work. She had the idea that if he were in general practice she would have more money to spend on the pleasures of society, and her daughter reflected her attitude by founding an antivivisection society. Emmet, Oliver Wendell Holmes, Dr. Joseph L. Miller, Sir Ronald Ross and Lord Lister survived their wives. The others enjoyed the state of matrimony the rest of their lives. Kelly and his wife died within a few hours of each other and the Halsteds within a few months. This is a better record than you would expect from vital statistics, for even as late as 1948 life expectancy for the husband was 40 years and for the wife 49 and their joint expectancy of life was 36 years. At the turn of the century, joint expectancy of life was only 28 years.

A doctor's life is a hard one with long and irregular hours and duties that are exacting and nerveracking. To make a home for him is a real job. It is significant that none of the wives in this study was jealous of her husband's patients.

Lady Osler was a beautiful example of uxorial helpfulness. In background and experience she was well qualified for she was a descendant of Paul Revere and was the widow of a famous Philadelphia physician when she married the lovable Osler. The ideal home that she created for him, first at 1 West Franklin Street in Baltimore and next at 13 Norham Gardens in Oxford, was known all over the world for its hospitality. During the first World War the Oxford home was familiarly called the "Open Arms." Visiting doctors, especially if they were from the United States or Canada, were always welcome, but they never interfered with Sir William's work. Whether they dropped in for tea, were invited for dinner or were house guests, Lady Osler saw to it that they did not break into Osler's routine. After a short but brilliant postprandial conversation Sir William would quietly slip away to his study and his lady would carry on so efficiently that he was not missed.

Laetitia Bredow, the daughter of a Stetkin physician, was reared in the Teutonic

atmosphere where *Kinder, Kuchen und Kirche* were the *summum bonum* of wifely virtues. She must have had a hard time making a home for Kelly with his snakes and other unattractive objects of his natural science collections, to say nothing of his innumerable books that overflowed all parts of the house. However, she succeeded, bore him nine children and raised all and, when Kelly died at the ripe old age of eighty-five, she followed him in a few hours. Their joint funeral was attended by eight of the nine children. The ninth was serving his country in the South Pacific.

What shall we say of the home making efforts of Caroline Hampton, a niece of General Wade Hampton of South Carolina, who married the shy and exacting Halsted in 1890. At that time he was 38 years of age, and set in his ways—and what ways! He had his shoes made in England and his shirts laundered in Paris. He was extremely critical of the behavior of people although not in the least intolerant, and he was witty and sarcastic. When he gave one of his exquisite dinners, he would select the coffee beans at the table, and grind them and brew the coffee himself. His wife would spend the next day in bed with the migraine. Suffice it to say that she made a success of her marriage, for they were devoted to each other, but the effort was exhausting and, when Halsted died in 1922 after 32 year of marriage, she died two months later of pneumonia.

Not infrequently the exacting task of home making was complicated by chronic illness. Theresa Jones, the boyhood sweetheart of Marion Sims, was the daughter of a wealthy physician in South Carolina. Thoroughbred is the only adjective that adequately describes her. Against her mother's wishes she married Sims, a poor doctor who began his medical life as a failure. In Alabama he had several attacks of malaria and just as he was attaining success, he developed a severe avitaminosis which modern experts think was pellagra. At least he had an uncontrollable diarrhea and mental symptoms which resisted all treatment. The only thing that benefited him was a change of climate. Theresa did not hesitate. She sold out everything in Montgomery and moved North. When they reached Philadelphia, Sims was not expected to live, and he wrote his epoch-making paper on vesico-vaginal fistula in a Philadelphia boarding house. It was published in the American Journal of the Medical Sciences in 1852. When his health improved they moved on to New York, and there, to make ends meet, she took in roomers. When success came Sims went to Europe where he practiced on queens and duchesses, and taught the European surgeons how to cure vesico-vaginal fistula. Theresa followed him to Paris and was as at home in the brilliant court of Napoleon III as she had been in her native South Carolina. She kept her mercurial husband on an even keel and, when Sims reached the end of his long road, they were still sweethearts as they had been in the beginning. Truly she deserved the Distinguished Service Medal in Medicine.

At the end of World War I, Harvey Cushing was seriously ill and developed thrombosis of both femoral arteries. Ever afterward he had trouble with his feet and legs, and at autopsy, the femoral arteries were found to be completely occluded. Nevertheless, Cushing continued at his accustomed furious pace and died of heart disease when he had completed his Biblical allotment of three score and ten years. How much Kate Crowell Cushing had to do with this outcome, there is no direct testimony. Undoubtedly she made his path smooth these many years.

In the case of George Minot and his diabetes, we have the testimony of his physician, Dr. E. P. Joslin. Marian Linzee Weld married Minot, in 1915. In 1921 it was discovered that he had diabetes. At that time there was no insulin treatment. "He never could have carried on without the support he received from his wife who for twenty-eight years softened the blow. It was she who protected every minute of his existence, his going out and his coming in. It was she who weighed his food and

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saved him from worry of the management of his disease, and she did it all in so unobtrusive a manner that neither he nor others realized it."

Emmet who lived to ninety-one complained bitterly of loneliness when he was left a widower in his last years. And so it was with the other wives who made the lives of their self-sacrificing husbands happy ones.

Henry Asbury Christian

1876-1951

IN THE death of Henry Asbury Christian, Virginia has lost a distinguished son and the world a great doctor. Even in his college days Henry Christian was outstanding. He moulded college opinion to an unusual degree. His tall, upstanding figure, his pleasant smile, his quiet dignity, and his sound common sense commanded respect all over the campus. Whenever a question arose the boys wanted to know, "What does Henry think about it?"

Henry Christian was born in Lynchburg, February 17, 1876, the son of Camillus and Mary Elizabeth (Davis) Christian. He was a lineal descendant of Thomas Christian who patented land in Virginia in 1657. He graduated from Randolph-Macon College in 1895 with the degrees of A.B. and A.M. and from Johns Hopkins in 1900 with an M.D. degree. He also earned an A.M. degree from Harvard in 1903. Jefferson Medical College and the University of Michigan conferred upon him the honorary degree of Sc.D. and Randolph-Macon, Western Reserve and the University of Western Ontario the honorary degree of Doctor of Laws.

Upon leaving Hopkins he followed the general pattern set by his great teacher, Sir William Osler, becoming first a pathologist, then a teacher of medicine, having several diseases—Schüller-Christian and Christian-Weber diseases—named for him, and finally, establishing a great teaching hospital, the Peter Bent Brigham Hospital. In this undertaking he was associated with Harvey Cushing, he as physician-in-chief and Cushing as surgeon-in-chief. Under the influence and guidance of these illustrious teachers the Brigham became one of the great hospitals of the world.

Dr. Christian's first position in Boston was assistant pathologist at the Boston City Hospital, later becoming assistant visiting pathologist. He was also assistant pathologist at the Children's Hospital and instructor in pathology at Harvard. From 1908 to 1912 he was dean of the faculty of medicine of Harvard and in 1908 he became the Hersey professor of the theory and practice of physic. He retired from this professorship in 1939, but was recalled in 1942 on account of the war. He was also clinical professor of medicine (1943) at Tufts, and physician-in-chief at the Carney Hospital (1907-12). He was a major in the medical reserve Corps of the U.S. Army from 1918 to 1921 and for one year was resident chairman of the division of medical sciences of the National Research Council.

At the Centennial Session of the American Medical Association, the House of Delegates awarded this eminent Virginian the Distinguished Service Medal for scientific advancement in the field of medicine today. Among his other notable honors are the presidency of the American Society for Clinical Investigation (1919), that of the Interstate Postgraduate Medical Association of North America (1931), and of the Association of American Physicians (1935). The *Monthly* is proud to number him among its outstanding contributors.

Dr. Christian died of heart disease at Whitfield, New Hampshire on Friday, August 24th and was buried from the Church of Our Savior in Brookline, Massachusetts, August 27th. He leaves a host of admirers among Virginia physicians.

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SOCIETY PROCEEDINGS

The Fourth District Medical Society

Met August the 29th, at the Masonic Lodge in Lawrenceville, under the presidency of Dr. L. H. Bracey of South Hill. Papers were presented by Richmond doctors as follows:

Backache—R. D. Butterworth, M.D.

The Nervous Patient—W. T. Thompson, M.D.

Poliomyelitis—Lee E. Sutton, Jr., M.D.

A business session followed, after which those present enjoyed a cocktail party and dinner. There was a Round Table discussion after dinner.

The meeting was sponsored in conjunction with the Department of Clinical and Medical Education of The Medical Society of Virginia. Dr. James A. Thweatt of Petersburg is secretary-treasurer, and Dr. A. Tyree Finch of Farmville chairman of the Steering Committee.

Joint Meeting

The Mid-Tidewater and Northern Neck Medical Societies held another joint meeting, September 26, at the Tappahannock Yacht Club. This was under the auspices of the Department of Clinical and Medical Education of The Medical Society of Virginia. Papers on the program were given by members of the staff of the Medical College of Virginia and were:

The Neurological Examination—Weir M. Tucker, M.D.

The Office Regulation of New Diabetics—William R. Jordan, M.D.

The Treatment of Hay Fever and Asthma—M. E. B. Owens, Jr., M.D.

Convulsions—Weir M. Tucker, M.D.

The Treatment of Diabetes with Infection—William R. Jordan, M.D.

An intermission was taken at 5:30 for cocktails and dinner.

NEWS

The 100th Anniversary of Dr. Walter Reed's Birth

Was celebrated at Gloucester, on September 13, when a number of people gathered to pay tribute to the conqueror of yellow fever. Business houses at Gloucester Courthouse and the Botetourt High School closed at noon that day to honor Dr. Reed. "Belroi", the birthplace of Dr. Reed was open all day but the exercises were held on the grounds of the High School because of limited parking space at "Belroi".

The program opened with a band concert on the school lawn at 1:15 p.m. by the Fiftieth Army Band of Fort Monroe. At two o'clock, the address of welcome was given by John Tabb DuVal, Commonwealth's attorney of Gloucester and former member of the Virginia House of Delegates. State Senator Marvin Minter of Mathews introduced the guest speakers, Dr. Wyndham B. Blanton, physician and historian of Richmond, and Major-General Paul H. Streit, commanding general of the Army Medical Center in Washington. Among the guests, in addition to members of Dr. Reed's family, was Dr. Robert P. Cooke of Lexington, who was one of the group who volunteered for Reed's experiments in Havana.

Greater Accuracy in Laboratory Diagnosis.

The College of American Pathologists announces the organization of a program to improve the efficiency and to increase the uniformity of medical laboratory analyses.

At first this program will function primarily in supplying highly standardized and very accurate solutions that will enable small and large pathology laboratories to develop and maintain uniformly reliable test solutions in the field of chemical determinations. By checking solutions prepared by their own technicians against the standard solutions supplied them, directors of medical laboratories can thereby increase the reliability of their medical tests.

The recent distribution of standardized dextrose and nitrogen solutions to 1450 member pathologists (who represent about 80 per cent of all certified pathologists) actually marks the initial step in the de-

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velopment of a comprehensive program for standardization of laboratory procedures.

State Health Commissioner.

Dr. Mack I. Shanholtz has been appointed by Governor Battle to succeed Dr. L. J. Roper deceased, as State Health Commissioner, effective October 1, 1951. Dr. Shanholtz is a graduate of the University of Virginia, Department of Medicine, in 1934, and later took his master's degree in public health work. He was connected with the Virginia State Health Department for several years before going to Oklahoma where he became director of the Seminole County health department and assistant professor of preventive medicine and public health at the University of Oklahoma School of Medicine.

Dr. A. L. Carson, Jr., has been designated to fill the vacancy created by the resignation of Dr. J. C. Neale, Jr., to serve as interim Director of the Division of Local Health Services until a permanent appointment can be made.

The Division of Specialized Medical Services will continue to be directed by Dr. Carson with the exception of the Bureau of Maternal and Child Health, the activities of which will be directed by Dr. L. L. Shamburger during this period.

The Post Graduate Clinical Sessions,

Sponsored by The Virginia Society of Ophthalmology and Otolaryngology, will be held in Richmond, at the Baruch Auditorium of the Medical College of Virginia, November 27, 28, 29 and 30, 1951. The first two days are for otolaryngology and the remaining two days for ophthalmology.

For further information inquiries may be addressed to P. N. Pastore, M.D., Chairman, Box 25, Medical College of Virginia Station, 1200 East Broad Street, Richmond 19.

Dr. J. C. Neale, Jr.,

Formerly director of Local Health Services with the State Department of Health, recently tendered his resignation and has accepted a position with the Veterans Administration Hospital at Mountain Home, Tennessee, where he will practice clinical medicine.

The American College of Chest Physicians

Will hold its Interim Session at the Ambassador Hotel, Los Angeles, on December 2 and 3, 1951. On December 2, a scientific session will be presented sponsored by the California Chapter of the College, including round table luncheon discussions and an x-ray conference. A banquet will be held in the evening. The Board of Regents of the American College of Chest Physicians will meet on December 3, as well as various councils and committees of the College.

Dr. Edward W. Hayes, Monrovia, California, is chairman of the general arrangements committee for the Interim Session of the College, and Dr. Alfred Goldman, Beverly Hills, is chairman of the scientific program committee.

The Piedmont Proctologic Society

Held its annual August meeting in Asheville, N. C., at the Battery Park Hotel. Dr. C. Ross Deeds of Hendersonville, N. C., president, presided over the business session and the election of officers for the coming year. Those elected were President, Dr. J. Milton Stockman of Knoxville, Tennessee; Vice-President, Dr. Charles S. Drummond of Winston-Salem, N. C.; and Secretary-Treasurer, Dr. B. Richard Jackson of Raleigh, N. C.

During the scientific session, the following papers were presented; "The Incidence of Postoperative Complications in Anorectal Surgery", by Dr. B. Richard Jackson, "Anesthesia in Proctologic Surgery", by Dr. William Galvin of Emory University Medical School, Atlanta, Ga., and "The Reduction of Postoperative Pain after Rectal Surgery", by Dr. Edgar Boling of Atlanta, Ga.

Parke-Davis Moves Latin America Headquarters.

W. R. Jeeves, director of overseas operations for Parke-Davis and Company, announces the establishment of a new Latin-America headquarters in the recently created free zone at Colon, Panama. From here, the Company will serve 14 Spanish-speaking countries, excluding the areas served by the branches at Buenos Aires, Rio de Janeiro, Mexico City and Havana. Edward Castano, who has been New York manager of Parke-Davis' Inter-American Corporation, will move to Colon in October and direct the new headquarters. Several key people will be transferred with him and they will train others who will be citizens of Panama and other Latin-America countries. About 30,000 physicians are to benefit from the new center.

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Dr. Waverly R. Payne,

Newport News, was among those recently appointed by Governor Battle to the Board of Visitors of the Medical College of Virginia.

Dr. Charles R. Woolwine,

Blacksburg, retired September 1 as the Virginia Polytechnic Institute health officer after twenty-three years of service to that institution. He plans to devote his time to the raising of cattle on his 160-acre farm.

American Medical Association—Winter Session.

Postgraduate study primarily designed for the general practitioner will be the theme of the 1951 Clinical Session of the American Medical Association to be held in Los Angeles, December 4 through 7. However, subjects of interest to the specialist will also be presented. Practical clinical discussions, scientific exhibits and general lectures on basic problems are planned.

Color television to demonstrate surgery, clinical treatment and examination procedure will be one of the highlights of the convention. The scientific and technical exhibits will be interesting and instructive and will be located in the Shrine Convention Hall, adjacent to the Al Malaikah Temple, where the lectures, clinical presentations, television reception and motion picture showings will take place.

Special interesting and diversified activities have been planned for physicians' wives as well as for the doctors.

More than 2,000 hotel rooms have been reserved for the session. Doctors, however, are urged to make their hotel reservations in advance by writing to Chairman, American Medical Association Subcommittee on Hotels, 1151 South Broadway, Los Angeles 15, Calif.

The American Association of Obstetricians, Gynecologists and Abdominal Surgeons

Held an instructive and pleasant meeting at Hot Springs, Va., September 6-8, under the presidency of Dr. James K. Quigley of Rochester, N. Y. At the close of the meeting, Dr. Leroy A. Calkins, Kansas City, Kansas, succeeded to the presidency. Others named to serve with him are: President-elect, Dr. Nicholson J. Eastman, Baltimore; treasurer, Dr. Frank R. Smith, New York City; secretary, Dr. William F. Mengert, Dallas; and assistant secretary, Dr. Frank R. Lock, Winston-Salem, N. C. The 1952 meeting will also be held at Hot Springs, the first week in September.

Dr. William Dunn Walker,

Class of '44, University of Virginia, Department of Medicine, after some time in Honolulu, is now located at 613 Grant Street, Charleston, West Virginia.

The American Dermatological Association

Again offers a prize of three hundred dollars for the best essay submitted for original work, not previously published, relative to some fundamental aspect of dermatology or syphilology.

Manuscripts typed in English with double spacing and ample margins as for publication together with illustrations, charts, and tables, all of which must be in *triplicate*, are to be submitted not later than December 1, 1951. They should be sent to Dr. Louis A. Brunsting, Secretary, American Dermatological Association, 102-110 Second Avenue, Southwest, Rochester, Minnesota.

The essays are judged on the following considerations: (1) originality of ideas; (2) potential importance of the work; (3) experimental methods and use of controls; (4) evaluation of results; (5) clarity of presentation; (6) historical background; (7) bibliography.

Further information regarding this essay contest may be obtained by writing to the secretary of the Association.

Medical College of Virginia News.

Dr. Paul S. Larson, research professor of pharmacology at the Medical College of Virginia and pharmacologist for the American Tobacco Company Research Laboratory, was one of the invited speakers at the American Chemical Society Jubilee in New York City in September. He presented a paper on the 6th in the symposium on the chemistry of tobacco entitled "Present Knowledge Concerning the Metabolism of Nicotine by the Animal Body and the Nature and Action of Tobacco Smoke Irritants". Immediately afterwards he and Mrs. Larson sailed for Europe. On September 20, Dr. Larson read a paper entitled "Studies on the Metabolism of Nicotine by the Animal Body" at the World Tobacco Congress in Amsterdam, Holland.

At the 12th International Congress of Pure and Applied Chemistry in New York, September 12, Dr.

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R. Blackwell Smith, Jr., dean of the School of Pharmacy and associate professor of pharmacology, presented a paper titled "Toxicological Studies on the Zinc and Disodium Salts of Ethylene-bis-dithio-carbamates". His research associates in this work were Doctors J. K. Finnegan, P. F. Sahyoun, H. B. Haag and Paul S. Larson..

Doctors G. Watson James, III, and Lynn D. Abbott, Jr., are authors of a paper which appeared in the July number of PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE. Their report has to do with the "Effectiveness of Thiocyanate Analog of Vitamin B_{12} in Pernicious Anemia."

The Annual Postgraduate Course in Diseases of the Chest,

Sponsored by the Council on Postgraduate Medical Education and the New York State Chapter of the American College of Chest Physicians, will be presented at the Hotel New Yorker, New York City, November 12-17, 1951.

This course will emphasize the recent advancements in the diagnosis and treatment of chest diseases. The course is open to all physicians, but the number of registrants will be limited. Tuition fee is $50.00; applications will be accepted in the order in which they are received by the American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Situation Wanted.

Young physician desires assistantship with general surgeon or general practitioner doing surgery; will consider general practice assistantship without surgery; eastern Virginia only. Write "Eastern Virginia", care Virginia Medical Monthly, 1105 West Franklin Street, Richmond 20, Va. (*Adv.*)

Wanted Doctor

At once for a small hospital in Southwest Virginia —either general practitioner or surgeon. Salary $1,000.00 per month, with maintenance for single man. Write "Hospital in Need", care this journal at 1105 West Franklin Street, Richmond 20. (*Adv.*)

Wanted—

Medical-Surgical partnership or location having or planning community hospital; will consider private hospital partnership. Write "Partnership", care this journal, 1105 West Franklin Street, Richmond 20. (*Adv.*)

OBITUARIES

Dr. Moses Benmosche,

Well known surgeon of New York City, died at his home there on September 4, after a short illness. He was born in London but studied medicine at the Medical College of Virginia, from which he graduated in 1904. After practicing in several places, he located in New York City in 1920, where he had been the recipient of many honors. He had been a member of The Medical Society of Virginia since 1912. His wife and two sons survive him.

Dr. William Warren Sager,

A surgeon at the McGuire Veterans Hospital, Richmond, died September 10, after a short illness. He was born in Shenandoah County, this State, fifty-three years ago, and received his diploma in medicine from George Washington University, Washington, in 1922. From 1929 to 1949 he was associate professor of clinical surgery at his alma mater. During World War II, he was chief of a general surgical section at the Navy Medical Center, Bethesda, Maryland, and later served on a Navy hospital ship. He joined the staff at McGuire's in 1949. He is survived by his wife and three children.

Dr. Thomas E. Knight,

Of Farmville, died August 16, at the age of forty-eight, after a short illness. He was a graduate of the Medical College of Virginia in 1929. He had practiced in Farmville since 1930. During World War II, he served in the Army Medical Corps.